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NEWS 4	JUL 28	IFICDB, IFIPAT, and IFIUDB reloaded with enhancements
NEWS 5	JUL 28	STN Viewer performance improved
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NEWS 9	AUG 15	CAplus currency for Korean patents enhanced
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NEWS 14	SEP 29	IFICLS enhanced with new super search field
NEWS 15	SEP 29	EMBASE and EMBAL enhanced with new search and display fields
NEWS 16	SEP 30	CAS patent coverage enhanced to include exemplified prophetic substances identified in new Japanese-language patents
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FILE 'HOME' ENTERED AT 09:25:54 ON 03 NOV 2008

=> file medline embase biosis scisearch caplus
COST IN U.S. DOLLARS   SINCE FILE   TOTAL
                                                         ENTRY   SESSION
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FILE 'MEDLINE' ENTERED AT 09:26:20 ON 03 NOV 2008

FILE 'EMBASE' ENTERED AT 09:26:20 ON 03 NOV 2008

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FILE 'SCISEARCH' ENTERED AT 09:26:20 ON 03 NOV 2008

FILE 'CAPLUS' ENTERED AT 09:26:20 ON 03 NOV 2008

=> s glycoconjugate?
L1   31789 GLYCOCONJUGATE?

=> s l1 and targeting
L2   478 L1 AND TARGETING

=> s l2 and therapeutic agent
L3   17 L2 AND THERAPEUTIC AGENT

=> s l3 and modified sugar
L4   0 L3 AND MODIFIED SUGAR

=> s l1 and therapeutic?
L5   1005 L1 AND THERAPEUTIC?

=> s l5 and modified saccharride
L6   0 L5 AND MODIFIED SACCHARRIDE

=> s l5 and galactose
L7   76 L5 AND GALACTOSE

=> s l7 and ketone
L8   0 L7 AND KETONE

=> s l7 and GalNAc

L9 5 L7 AND GALNAC

=> s l9 and O-linked
L10 0 L9 AND O-LINKED

=> dup remove l9
PROCESSING COMPLETED FOR L9
L11 5 DUP REMOVE L9 (0 DUPLICATES REMOVED)

=> s l11 and pd<20031119
1 FILES SEARCHED...
4 FILES SEARCHED...
L12 1 L11 AND PD<20031119

=> d l12 cbib abs

L12 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2008 ACS on STN
2005:122585 Document No. 142:217398 Cell-free in vitro glycoconjugation of interleukin 2 as **therapeutic** agent against cancer and AIDS in mammal and human. Defrees, Shawn; Zopf, David; Bayer, Robert; Bowe, Caryn; Hakes, David; Chen, Xi (Neose Technologies, Inc., USA). U.S. Pat. Appl. Publ. US 20050031584 A1 20050210, 750 pp., Cont.-in-part of U.S. Ser. No. 360,779. (English). CODEN: USXXCO. APPLICATION: US 2003-410980 20030409. PRIORITY: US 2001-328523P 20011010; US 2001-344692P 20011019; US 2001-334301P 20011128; US 2001-334233P 20011128; US 2002-387292P 20020607; US 2002-391777P 20020625; US 2002-396594P 20020717; US 2002-404249P 20020816; US 2002-407527P 20020828; WO 2002-US32263 20021009; US 2002-287994 20021105; US 2003-360770 20030106; US 2003-360779 20030219.

AB The invention includes methods and compns. for remodeling a peptide mol., including the addition or deletion of one or more glycosyl groups to a peptide, and/or the addition of a modifying group to a peptide. The method uses enzyme to remove or add phosphate, sulfate, carboxylate and/or ester group-containing saccharide to interleukin 2 peptide, and then conjugate the saccharide-linked interleukin 2 with modifying group such as polymer, **therapeutic** moiety, detectable label, toxin, radioisotope, targeting moiety and peptide. The saccharide group comprises monosaccharyl, oligosaccharyl, glycosyl, truncated glycan, mannosyl, GlcNAc, xylosyl, sialyl, galactosyl, glucosyl or **GalNAc**. The enzyme for the saccharide addition or removal is a prokaryotic or eukaryotic glycosyltransferase selected from sialyltransferase, galactosyltransferase, glucosyltransferase, **GalNAc** transferase, GlcNAc transferase, fucosyltransferase, mannosyltransferase, endo-N-acetylgalactosaminidase, glycosidase, sialidase, mannosidase, etc. The substrate is a nucleotide sugar such as UDP-glucose, UDP-**galactose**, UDP-galactosamine, UDP-glucosamine, UDP-N-acetylgalactosamine, UDP-N-acetylglucosamine, GDP-mannose, GDP-fucose, CMP-sialic acid and CMP-NeuAc.

=> s l2 and 2-N-Acetamidosugars
L13 1 L2 AND 2-N-ACETAMIDOSUGARS

=> d l13 cbib abs

L13 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2008 ACS on STN
2001:52655 Document No. 134:248403 Ketone Isosteres of **2-N-Acetamidosugars** as Substrates for Metabolic Cell Surface Engineering. Hang, Howard C.; Bertozzi, Carolyn R. (Departments of Chemistry, University of California, Berkeley, CA, 94720, USA). Journal of the American Chemical Society, 123(6), 1242-1243 (English) 2001. CODEN: JACSAT. ISSN: 0002-7863. OTHER SOURCES: CASREACT 134:248403. Publisher: American Chemical Society.

AB Metabolic oligosaccharide engineering using unnatural substrates has provided an avenue for the introduction of novel chemical reactivity on cell surfaces. This approach exploits the unnatural substrate tolerance of enzymes involved in carbohydrate biosynthesis. For example, derivs. of N-acetylmannosamine (ManNAc) which bear a selectively reactive chemical handle, such as a ketone or azide, on the N-acyl group are transformed into **glycoconjugate**-bound sialosides by human cells. The selective reactivity of ketones with aminooxy or hydrazide groups, and azides with modified phosphine reagents, permits exogenous chemical cell surface **targeting.** If the substrate promiscuity exhibited by the enzymes and transporters of the sialic acid pathway is a general feature of other carbohydrate metabolic pathways, multiple avenues for metabolic engineering will be available. So far, few studies have addressed the unnatural substrate tolerance of other carbohydrate biosynthetic pathways. The ubiquitous presence of the **2-N-acetamidosugars**, N-acetylglucosamine (GlcNAc) and N-acetylgalactosamine (GalNAc), in glycoproteins, proteoglycans, and glycolipids makes them attractive targets for metabolic engineering. GlcNAc and GalNAc are converted within cells to their UDP-activated analogs via salvage pathways. UDP-GlcNAc can be subsequently converted to ManNAc or UDP-GalNAc, or utilized by GlcNAc transferases that incorporate the sugar into various **glycoconjugates.** Likewise, GalNAc transferases utilize UDP-GalNAc as a substrate and deliver the sugar to numerous **glycoconjugates.** We considered the possibility that unnatural GlcNAc and GalNAc derivs. might gain access to the cell surface through their resp. salvage pathways. We designed 2-ketosugars, which are C2-carbon isosteres of the **2-N-acetamidosugars**, as novel analogs that possess a ketone group for chemoselective reaction with aminooxy or hydrazide reagents. A concise synthesis of 2-ketosugars was developed from known 2-iodosugars, which are readily available by electrophilic iodination of com. available glycals. The cellular metabolism of the 2-ketosugars was investigated in a number of cell lines which exhibit varying patterns of N- and O-linked glycosylation. In conclusion, we have demonstrated that a 2-keto isostere of GalNAc is a novel substrate for metabolic glycoprotein engineering in wild-type and ldl-D CHO cells. The corresponding GlcNAc analog could not be detected on cells of any type, perhaps due to competition with endogenous GlcNAc and its downstream intermediates in the salvage pathway which are present at notoriously high intracellular concns. The 2-keto GalNAc analog should be incorporated into secreted glycoproteins as well as cell surface mols., since both are similarly post-translationally modified. This technique might be exploited to introduce unique chemical reactivity into secreted glycoproteins produced by large-scale recombinant expression, allowing further selective modification.

```
=> s l2 and ketone
L14          9 L2 AND KETONE

=> s l14 and C-2 position
L15          0 L14 AND C-2 POSITION

=> s l14 and 2N-acetyl
L16          0 L14 AND 2N-ACETYL

=> dup remove l14
PROCESSING COMPLETED FOR L14
L17           5 DUP REMOVE L14 (4 DUPLICATES REMOVED)

=> d l17 1-5 cbib abs

L17  ANSWER 1 OF 5  CAPLUS  COPYRIGHT 2008 ACS on STN
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2007:321112 Document No. 146:517239 Direct Identification of Nonreducing GlcNAc Residues on N-Glycans of Glycoproteins Using a Novel Chemoenzymatic Method. Boeggeman, Elizabeth; Ramakrishnan, Boopathy; Kilgore, Charlton; Khidekel, Nelly; Hsieh-Wilson, Linda C.; Simpson, John T.; Qasba, Pradman K. (Structural Glycobiology Section, CCR-Nanobiology Program, Center for Cancer Research, NCI-Frederick, Frederick, MD, 21702, USA). Bioconjugate Chemistry, 18(3), 806-814 (English) 2007. CODEN: BCCHES. ISSN: 1043-1802. Publisher: American Chemical Society.

AB The mutant β1,4-galactosyltransferase (β4Gal-T1), β4Gal-T1-Y289L, in contrast to wild-type β4Gal-T1, can transfer GalNAc from the sugar donor UDP-GalNAc to the acceptor, GlcNAc, with efficiency as good as that of galactose from UDP-Gal. Furthermore, the mutant can also transfer a modified sugar, C2 keto galactose, from its UDP derivative to O-GlcNAc modification on proteins that provided a functional handle for developing a highly sensitive chemoenzymic method for detecting O-GlcNAc post-translational modification on proteins. We report herein that the modified sugar, C2 keto galactose, can be transferred to free GlcNAc residues on N-linked glycoproteins, such as ovalbumin or asialo-agalacto IgG1. The transfer is strictly dependent on the presence of both the mutant enzyme and the **ketone** derivative of the galactose. Moreover, the PNGase F treatment of the glycoproteins, which cleaves the N-linked oligosaccharide chain, shows that the modified sugar has been transferred to the N-glycan chains of the glycoproteins and not to the protein portion. The application of the mutant galactosyltransferase, β4Gal-T1-Y289L, to produce **glycoconjugates** carrying sugar moieties with reactive groups, is demonstrated. We envision a broad potential for this technol. such as the possibilities to link cargo mols. to glycoproteins, such as monoclonal antibodies, via glycan chains, thereby assisting in the glyco-**targeting** of drugs to the site of action or used as biol. probes.

L17 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN

2001:52655 Document No. 134:248403 **Ketone** Isosteres of 2-N-Acetamidosugars as Substrates for Metabolic Cell Surface Engineering. Hang, Howard C.; Bertozzi, Carolyn R. (Departments of Chemistry, University of California, Berkeley, CA, 94720, USA). Journal of the American Chemical Society, 123(6), 1242-1243 (English) 2001. CODEN: JACSAT. ISSN: 0002-7863. OTHER SOURCES: CASREACT 134:248403. Publisher: American Chemical Society.

AB Metabolic oligosaccharide engineering using unnatural substrates has provided an avenue for the introduction of novel chemical reactivity on cell surfaces. This approach exploits the unnatural substrate tolerance of enzymes involved in carbohydrate biosynthesis. For example, derivs. of N-acetylmannosamine (ManNAc) which bear a selectively reactive chemical handle, such as a **ketone** or azide, on the N-acyl group are transformed into **glycoconjugate**-bound sialosides by human cells. The selective reactivity of **ketones** with aminooxy or hydrazide groups, and azides with modified phosphine reagents, permits exogenous chemical cell surface **targeting**. If the substrate promiscuity exhibited by the enzymes and transporters of the sialic acid pathway is a general feature of other carbohydrate metabolic pathways, multiple avenues for metabolic engineering will be available. So far, few studies have addressed the unnatural substrate tolerance of other carbohydrate biosynthetic pathways. The ubiquitous presence of the 2-N-acetamidosugars, N-acetylglucosamine (GlcNAc) and N-acetylgalactosamine (GalNAc), in glycoproteins, proteoglycans, and glycolipids makes them attractive targets for metabolic engineering. GlcNAc and GalNAc are converted within cells to their UDP-activated analogs via salvage pathways. UDP-GlcNAc can be subsequently converted to ManNAc or UDP-GalNAc, or utilized by GlcNAc transferases that incorporate the sugar into various **glycoconjugates**. Likewise, GalNAc transferases utilize UDP-GalNAc as a substrate and deliver the sugar to

numerous **glycoconjugates**. We considered the possibility that unnatural GlcNAc and GalNAc derivs. might gain access to the cell surface through their resp. salvage pathways. We designed 2-ketosugars, which are C2-carbon isosteres of the 2-N-acetamidosugars, as novel analogs that possess a **ketone** group for chemoselective reaction with aminooxy or hydrazide reagents. A concise synthesis of 2-ketosugars was developed from known 2-iodosugars, which are readily available by electrophilic iodination of com. available glycals. The cellular metabolism of the 2-ketosugars was investigated in a number of cell lines which exhibit varying patterns of N- and O-linked glycosylation. In conclusion, we have demonstrated that a 2-keto isostere of GalNAc is a novel substrate for metabolic glycoprotein engineering in wild-type and ldl-D CHO cells. The corresponding GlcNAc analog could not be detected on cells of any type, perhaps due to competition with endogenous GlcNAc and its downstream intermediates in the salvage pathway which are present at notoriously high intracellular concns. The 2-keto GalNAc analog should be incorporated into secreted glycoproteins as well as cell surface mols., since both are similarly post-translationally modified. This technique might be exploited to introduce unique chemical reactivity into secreted glycoproteins produced by large-scale recombinant expression, allowing further selective modification.

L17 ANSWER 3 OF 5 MEDLINE on STN DUPLICATE 1

2002001735. PubMed ID: 11750762. Kinetic parameters for small-molecule drug delivery by covalent cell surface **targeting**. Nauman D A; Bertozzi C R. (Department of Chemistry, University of California-Berkeley, Berkeley, CA 94720, USA.) Biochimica et biophysica acta, (2001 Dec 5) Vol. 1568, No. 2, pp. 147-54. Journal code: 0217513. ISSN: 0006-3002. Pub. country: Netherlands. Language: English.

AB Human cells incubated with N-levulinoylmannosamine (ManLev) process this unnatural metabolic precursor into N-levulinoyl sialic acid (SiaLev), which is incorporated into cell surface **glycoconjugates**. A key feature of SiaLev is the presence of a **ketone** group that can be exploited in chemoselective ligation reactions to deliver small-molecule probes to the cell surface. A mathematical model was developed and tested experimentally to evaluate the prospects of using cell surface **ketones** as targets for covalent small-molecule drug delivery. We quantified the absolute number of **ketone** groups displayed on cell surfaces as a function of the concentration of ManLev in the medium. The apparent rate constants for the hydrolysis and disappearance of the cell surface conjugates were determined, as well as the apparent rate constant for the formation of covalent bonds with cell surface **ketones**. These values and the mathematical model confirm that chemoselective reactions on the cell surface can deliver to cells similar numbers of molecules as antibodies. Thus, cell surface **ketones** are a potential vehicle for a metabolically controlled small-molecule drug delivery system.

L17 ANSWER 4 OF 5 EMBASE

2001150802 EMBASE Biochemical engineering of the N-acyl side chain of sialic acid: Biological implications.

Keppler, O.T.; Horstkorte, R.; Pawlita, M.; Schmidt, C.; Reutter, W. (correspondence). Inst. Molekularbiologie Biochemie, Fachbereich Humanmedizin, Freie Universitat Berlin, Arnimallee 22, D-14195 Berlin-Dahlem, Germany.

Glycobiology Vol. 11, No. 2, pp. 11R-18R 2001.
Refs: 43.
ISSN: 0959-6658. CODEN: GLYCE3.
Pub. Country: United Kingdom. Language: English. Summary Language: English.
Entered STN: 20010510. Last Updated on STN: 20010510

AB N-Acetylneuraminic acid is the most prominent sialic acid in eukaryotes. The structural diversity of sialic acid is exploited by viruses, bacteria, and toxins and by the sialoglycoproteins and sialogylcolipids involved in cell-cell recognition in their highly specific recognition and binding to cellular receptors. The physiological precursor of all sialic acids is N-acetyl D-mannosamine (ManNAc). By recent findings it could be shown that synthetic N-acyl-modified D-mannosamines can be taken up by cells and efficiently metabolized to the respective N-acyl-modified neuraminic acids in vitro and in vivo. Successfully employed D-mannosamines with modified N-acyl side chains include N-propanoyl- (ManNProp), N-butanoyl- (ManNBut)-, N-pentanoyl- (ManNPent), N-hexanoyl- (ManNHex), N-crotonoyl- (ManNCrot), N-levulinoyl- (ManNLev), N-glycolyl-(ManNGc), and N-azidoacetyl D-mannosamine (ManNAc-azido). All of these compounds are metabolized by the promiscuous sialic acid biosynthetic pathway and are incorporated into cell surface sialoglycoconjugates replacing in a cell type-specific manner 10-85% of normal sialic acids. Application of these compounds to different biological systems has revealed important and unexpected functions of the N-acyl side chain of sialic acids, including its crucial role for the interaction of different viruses with their sialylated host cell receptors. Also, treatment with ManNProp, which contains only one additional methylene group compared to the physiological precursor ManNAc, induced proliferation of astrocytes, microglia, and peripheral T-lymphocytes. Unique, chemically reactive **ketone** and azido groups can be introduced biosynthetically into cell surface sialoglycans using N-acyl-modified sialic acid precursors, a process offering a variety of applications including the generation of artificial cellular receptors for viral gene delivery. This group of novel sialic acid precursors enabled studies on sialic acid modifications on the surface of living cells and has improved our understanding of carbohydrate receptors in their native environment. The biochemical engineering of the side chain of sialic acid offers new tools to study its biological relevance and to exploit it as a tag for therapeutic and diagnostic applications.

L17 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
1997:158946 Engineering novel cell surface chemistry for selective tumor cell **targeting**.. Bertozzi, Carolyn R. (Lawrence Berkely National Laboratories, University California, Berkeley, CA, 94720, USA). Book of Abstracts, 213th ACS National Meeting, San Francisco, April 13-17, CARB-013. American Chemical Society: Washington, D. C. (English) 1997. CODEN: 64AOAA.

AB A common feature of many different cancers is the high expression level of the two monosaccharides sialic acid and fucose within the context of cell-surface associated **glycoconjugates**. A correlation has been made between hypersialylation and/or hyperfucosylation and the highly metastatic phenotype. Thus, a **targeting** strategy based on sialic acid or fucose expression would be a powerful tool for the development of new cancer cell-selective therapies and diagnostic agents. We have discovered that **ketone** groups can be incorporated metabolically into cell-surface associated sialic acids. The **ketone** is chemical unique to the cell surface and can be covalently ligated with hydrazide functionalized proteins or small mols. under physiol. conditions. Thus, we have discovered a mechanism to selectively target hydrazide conjugates to highly sialylated cells such as cancer cells. Applications of this technol. to the generation of novel cancer cell-selective toxins and MRI contrast reagents will be discussed, in addition to progress towards the use of cell surface fucose residues as vehicles for **ketone** expression.

=> s l2 and galactose
L18 74 L2 AND GALACTOSE

=> s l18 and amino group
L19 5 L18 AND AMINO GROUP

=> dup remove l19
PROCESSING COMPLETED FOR L19
L20 1 DUP REMOVE L19 (4 DUPLICATES REMOVED)

=> d l20 cbib abs

L20 ANSWER 1 OF 1 MEDLINE on STN DUPLICATE 1
1994264691. PubMed ID: 8205127. Tissue-**targeting** ability of saccharide-poly(L-lysine) conjugates. Gonsho A; Irie K; Susaki H; Iwasawa H; Okuno S; Sugawara T. (Drug Delivery System Institute, Ltd., Science University of Tokyo, Chiba, Japan.) Biological & pharmaceutical bulletin, (1994 Feb) Vol. 17, No. 2, pp. 275-82. Journal code: 9311984. ISSN: 0918-6158. Pub. country: Japan. Language: English.
AB To evaluate the effect of introducing a saccharide moiety to poly(amino acids) on tissue distribution, several **glycoconjugates** of epsilon-(2-methoxyethoxyacetyl)-poly(L-lysine) of three molecular weights were synthesized using an octylene spacer between the sugar and polymer chain. Methoxyethoxyacetylation of the epsilon-**amino group** of the lysine unit in poly(L-lysine) was useful for avoiding nonspecific distribution to many tissues as the result of cationic charges. The tissue-**targeting** ability of each saccharide moiety was considered as the actual amount changed in each tissue caused by saccharide modification. **Galactose** terminated saccharides such as **galactose**, lactose and N-acetylgalactosamine accumulated exclusively in the liver, probably by the hepatic receptor. These conjugates could therefore be good carriers for a drug delivery system to the liver. On the other hand, the mannosyl and fucosyl conjugates were preferentially delivered to the reticuloendothelial systems such as those in the liver, spleen and bone marrow. In particular, fucosyl conjugates accumulated more in the bone marrow than in the spleen. Xylosyl conjugates accumulated mostly in the liver and lung. Generally, the accumulated amount in the target tissue increased with increasing molecular weight and an increased number of saccharides on one molecule of polymer.

=> s l18 and hydroxyl group
L21 0 L18 AND HYDROXYL GROUP

=> s l18 and carboxyl
L22 1 L18 AND CARBOXYL

=> d l22 cbib abs

L22 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2008 ACS on STN
2005:122585 Document No. 142:217398 Cell-free in vitro glycoconjugation of interleukin 2 as therapeutic agent against cancer and AIDS in mammal and human. Defrees, Shawn; Zopf, David; Bayer, Robert; Bowe, Caryn; Hakes, David; Chen, Xi (Neose Technologies, Inc., USA). U.S. Pat. Appl. Publ. US 20050031584 A1 20050210, 750 pp., Cont.-in-part of U.S. Ser. No. 360,779. (English). CODEN: USXXCO. APPLICATION: US 2003-410980 20030409. PRIORITY: US 2001-328523P 20011010; US 2001-344692P 20011019; US 2001-334301P 20011128; US 2001-334233P 20011128; US 2002-387292P 20020607; US 2002-391777P 20020625; US 2002-396594P 20020717; US 2002-404249P 20020816; US 2002-407527P 20020828; WO 2002-US32263 20021009; US 2002-287994 20021105; US 2003-360770 20030106; US 2003-360779 20030219.
AB The invention includes methods and compns. for remodeling a peptide mol., including the addition or deletion of one or more glycosyl groups to a

peptide, and/or the addition of a modifying group to a peptide. The method uses enzyme to remove or add phosphate, sulfate, carboxylate and/or ester group-containing saccharide to interleukin 2 peptide, and then conjugate the saccharide-linked interleukin 2 with modifying group such as polymer, therapeutic moiety, detectable label, toxin, radioisotope, **targeting** moiety and peptide. The saccharide group comprises monosaccharyl, oligosaccharyl, glycosyl, truncated glycan, mannosyl, GlcNAc, xylosyl, sialyl, galactosyl, glucosyl or GalNAc. The enzyme for the saccharide addition or removal is a prokaryotic or eukaryotic glycosyltransferase selected from sialyltransferase, galactosyltransferase, glucosyltransferase, GalNAc transferase, GlcNAc transferase, fucosyltransferase, mannosyltransferase, endo-N-acetylgalactosaminidase, glycosidase, sialidase, mannosidase, etc. The substrate is a nucleotide sugar such as UDP-glucose, UDP-**galactose**, UDP-galactosamine, UDP-glucosamine, UDP-N-acetylgalactosamine, UDP-N-acetylglucosamine, GDP-mannose, GDP-fucose, CMP-sialic acid and CMP-NeuAc.

```
=> s l18 and hydroxyl
L23          0 L18 AND HYDROXYL

=> s l18 and thiol
L24          0 L18 AND THIOL

=> s l18 and phosphate
L25          6 L18 AND PHOSPHATE

=> dup remove l25
PROCESSING COMPLETED FOR L25
L26           6 DUP REMOVE L25 (0 DUPLICATES REMOVED)

=> d l26 1-6 cbib abs

L26  ANSWER 1 OF 6  EMBASE  COPYRIGHT (c) 2008 Elsevier B.V. All rights
     reserved on STN
2007034665  EMBASE  Oligosaccharides, neoglycoproteins and humanized plastics:
     Their biocatalytic synthesis and possible medical applications.
     Nahalka, Jozef (correspondence); Gemeiner, Peter. Institute of Chemistry,
     Slovak Academy of Sciences, Dubravska cesta 9, SK-845 38 Bratislava,
     Slovakia. nahalka@savba.sk. Shao, Jun. Ilypsa, Inc., 3406 Central
     Expressway, Santa Clara, CA 95051, United States.
     Biotechnology and Applied Biochemistry  Vol. 46, No. 1, pp. 1-12  Jan
     2007.
     Refs: 97.
     ISSN: 0885-4513. CODEN: BABIEC.
     Pub. Country: United Kingdom. Language: English. Summary Language:
     English.
     Entered STN: 20070220. Last Updated on STN: 20070220
AB   Glycobiology has become one of the fastest growing branches of the
     biological sciences.  Glycomics, which is the study of an organism's
     entire array of oligosaccharides, is now emerging as the third informatics
     wave after genomics and proteomics.  For example, it is possible to see
     this progress in the KEGG (Kyoto Encyclopedia of Genes and Genomes)
     database (http://www.genome.jp/ kegg/pathway/map/map01110.html).  The
     interest in this area stems from the realization that carbohydrates,
     especially oligosaccharides, and their interactions with proteins, play
     diverse informative roles in all organisms, and that more than half of all
     proteins are glycosylated.  When the biological and pharmaceutical
     importance of glycoconjugates is considered, it is surprising
     how little glycobiotechnology has developed.  This review reports the
     latest developments in the biocatalytic synthesis of oligosaccharides and
```

glycoconjugates, with special attention paid to the glycosyltransferase approach. The second part of the review takes the 'conceptual approach' and covers possible medical applications of synthesized **glycoconjugates**. Various new examples of the conjugation of glyco-informative saccharide sequence to known pharmaceuticals or biomaterials are cited. .COPYRGT. 2007 Portland Press Ltd.

L26 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
2005:216712 Document No. 142:292453 Nanoparticulate complexes of double-stranded nucleic acids and melamine derivatives for delivery of nucleic acids, including siRNA. Quay, Steven C.; Cui, Kunyuan; Dattilo, James W. (Nastech Pharmaceutical Company Inc., USA). PCT Int. Appl. WO 2005021044 A2 20050310, 45 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-US27806 20040825. PRIORITY: US 2003-497740P 20030825.
AB Nanoparticles of double-stranded nucleic acid complexed with a complexing agent, especially melamine derivs. 2,4,6-triguanidotriazine (I) and 2,4,6-triamidosarcosylmelamine (II), that form complexes with the nucleic acids are described for delivery of nucleic acids, especially siRNA, to a target organism, e.g. in treatment of disease. Each of these mols. can bind to three **phosphate** groups, allowing each mol. of I or II to bind up to three mols. of nucleic acids. The complex may be further stabilized by complexing with poly-L-arginine or a copolymer of L-glutamine and L-asparagine. The polyaminoacid may in turn be conjugated with **targeting** moieties. In a preferred embodiment, the nucleic acid is a double stranded RNA having 15 to 30 base pairs suitable for RNA interference. In another aspect of the invention, a dsRNA is produced in which all of the uridines are changed to 5-methyluridine (ribothymidine.). Preferably, the resultant dsRNAs have 15 to about 30 base pairs and are suitable for RNA interference. Ribothymidine-containing siRNA is effect in gene silencing and is stable to the RNAses of rat blood plasma. Synthesis of the melamine derivs. is described.

L26 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
2005:122585 Document No. 142:217398 Cell-free in vitro glycoconjugation of interleukin 2 as therapeutic agent against cancer and AIDS in mammal and human. Defrees, Shawn; Zopf, David; Bayer, Robert; Bowe, Caryn; Hakes, David; Chen, Xi (Neose Technologies, Inc., USA). U.S. Pat. Appl. Publ. US 20050031584 A1 20050210, 750 pp., Cont.-in-part of U.S. Ser. No. 360,779. (English). CODEN: USXXCO. APPLICATION: US 2003-410980 20030409. PRIORITY: US 2001-328523P 20011010; US 2001-344692P 20011019; US 2001-334301P 20011128; US 2001-334233P 20011128; US 2002-387292P 20020607; US 2002-391777P 20020625; US 2002-396594P 20020717; US 2002-404249P 20020816; US 2002-407527P 20020828; WO 2002-US32263 20021009; US 2002-287994 20021105; US 2003-360770 20030106; US 2003-360779 20030219.
AB The invention includes methods and compns. for remodeling a peptide mol., including the addition or deletion of one or more glycosyl groups to a peptide, and/or the addition of a modifying group to a peptide. The method uses enzyme to remove or add **phosphate**, sulfate, carboxylate and/or ester group-containing saccharide to interleukin 2 peptide, and then conjugate the saccharide-linked interleukin 2 with modifying group such as polymer, therapeutic moiety, detectable label, toxin, radioisotope, **targeting** moiety and peptide. The saccharide group comprises

monosaccharyl, oligosaccharyl, glycosyl, truncated glycan, mannosyl, GlcNAc, xylosyl, sialyl, galactosyl, glucosyl or GalNAc. The enzyme for the saccharide addition or removal is a prokaryotic or eukaryotic glycosyltransferase selected from sialyltransferase, galactosyltransferase, glucosyltransferase, GalNAc transferase, GlcNAc transferase, fucosyltransferase, mannosyltransferase, endo-N-acetylgalactosaminidase, glycosidase, sialidase, mannosidase, etc. The substrate is a nucleotide sugar such as UDP-glucose, UDP-**galactose**, UDP-galactosamine, UDP-glucosamine, UDP-N-acetylgalactosamine, UDP-N-acetylglucosamine, GDP-mannose, GDP-fucose, CMP-sialic acid and CMP-NeuAc.

L26 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
2004:182383 Document No. 140:231203 Methods for cell-free remodeling and glycoconjugation of glycopeptides, remodeling of α-galactosidase A peptides, and their therapeutic use for Fabry disease. Defrees, Shawn; Zopf, David; Bayer, Robert; Bowe, Caryn; Hakes, David; Chen, Xi (Neose Technologies, Inc., USA). U.S. Pat. Appl. Publ. US 20040043446 A1 20040304, 761 pp., Cont.-in-part of Appl. No. PCT/US02/32263. (English). CODEN: USXXCO. APPLICATION: US 2003-411037 20030409. PRIORITY: US 2002-2002/PV38729U 20020607; US 2002-2002/PV39177U 20020625; US 2002-2002/PV39659U 20020717; US 2002-2002/PV40424U 20020816; US 2002-2002/PV40752W 20020828; WO 2002-US32263 20021009.

AB The invention includes methods and compns. for remodeling a peptide mol., including the addition or deletion of one or more glycosyl groups to a peptide, and/or the addition of a modifying group to a peptide. The invention claims a method of remodeling an α-galactosidase A peptide in vitro by removing a saccharyl subunit from the peptide and contacting the truncated glycan with at least one glycosyltransferase and a glycosyl donor to transfer the glycosyl donor to the glycan moiety. The glycosyl donor may contain a modifying group such as a polymer, a therapeutic toxin, a detectable label, a reactive linker group, or a **targeting** mol. The invention specifically claims α-galactosidase glycopeptides containing mannooligosaccharide or sialyloligosaccharide structures and their modification with a galactosyltransferase, a sialyltransferase, or a mannosyltransferase and modified glycosyl donors such as UDP-Gal-polyethylene glycol (PEG)-transferrin , CMP-sialic acid linker-mannose-6-**phosphate**, CMP-sialic acid-PEG, or GDP-mannose-linker-ApoE. Conjugation of glycopeptides with PEG, for example, is intended to reduce the immunogenicity of peptides and prolong their half-life in circulation. Conjugation of glycopeptides with transferrin is intended to transport **glycoconjugates** across the blood-brain barrier. In addition, the invention claims therapeutic use of a **glycoconjugated** α-galactosidase A peptide for Fabry disease. Examples of the invention include synthesis of CMP-sialic acid, UDP-**galactose**, UDP-glucosamine, and UDP-galactosamine conjugates with polyethylene glycol, sialylation of recombinant glycoproteins antithrombin III, fetuin, and α1-antitrypsin by recombinant rat ST3Gal III, and glyco-remodeling of Cri-IgG1 monoclonal antibody. The general procedure for making UDP-GlcNAc-PEG is that the protected amino sugar diphospho-nucleotide is oxidized to form an aldehyde at the 6-position of the sugar. The aldehyde is converted to the corresponding primary amine by formation and reduction of the Schiff base. The resulting intermediate is contacted with the p-nitrophenol carbonate of m-PEG, which reacts with the amine, binding the m-PEG to the saccharide via an amide bond.

L26 ANSWER 5 OF 6 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
2003458168 EMBASE Specificity and Mechanism of Metal Ion Activation in UDP-**galactose**:β -Galactoside-α-1,3-galactosyltransferase.
Zhang, Yingnan; Brew, Keith (correspondence). Dept. of Biochem. and Molec. Biology, Univ. of Miami School of Medicine, Miami, FL 33101, United States

. kbrew@fav.edu. Wang, Peng G.. Department of Chemistry, Wayne State University, Detroit, MI 48202, United States. Brew, Keith (correspondence). Dept. of Biomedical Sciences, Florida Atlantic University, 777 Glades Rd., Boca Raton, FL 33431, United States. kbrew@fav.edu.
Journal of Biological Chemistry Vol. 276, No. 15, pp. 11567-11574 13 Apr 2001.
Refs: 48.
ISSN: 0021-9258. CODEN: JBCHA3.
Pub. Country: United States. Language: English. Summary Language: English.
Entered STN: 20031204. Last Updated on STN: 20031204

AB UDP-**galactose**:β-galactosyl-α1,3-galactosyltransferase (α3GT) catalyzes the synthesis of galactosyl-α-1, 3-β-galactosyl structures in mammalian **glycoconjugates**. In humans the gene for α3GT is inactivated, and its product, the α-Gal epitope, is the target of a large fraction of natural antibodies. α3GT is a member of a family of metal-dependent-retaining glycosyltransferases that includes the histo blood group A and B enzymes. Mn(2+) activates the catalytic domain of α3GT (α3GTcd), but the affinity reported for this ion is very low relative to physiological levels. Enzyme activity over a wide range of metal ion concentrations indicates a dependence on Mn(2+) binding to two sites. At physiological metal ion concentrations, Zn(2+) gives higher levels of activity and may be the natural cofactor. To determine the role of the cation, metal activation was perturbed by substituting Co (2+) and Zn(2+) for Mn(2+) and by mutagenesis of a conserved D(149)VD(151) sequence motif that is considered to act in cation binding in many glycosyltransferases. The aspartates of this motif were found to be essential for activity, and the kinetic properties of a Val(150) to Ala mutant with reduced activity were determined. The results indicate that the cofactor is involved in binding UDP-**galactose** and has a crucial influence on catalytic efficiency for **galactose** transfer and for the low endogenous UDP-**galactose** hydrolase activity. It may therefore interact with one or more **phosphates** of UDP-**galactose** in the Michaelis complex and in the transition state for cleavage of the UDP to **galactose** bond. The DXD motif conserved in many glycosyltransferases appears to have a key role in metal-mediated donor substrate binding and **phosphate**-sugar bond cleavage.

L26 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
1987:596522 Document No. 107:196522 Original Reference No. 107:31517a,31520a
The use of glycoside aglycones to control the regioselectivity of glycosidic bond formation during enzymic oligosaccharide synthesis. Nilsson, Kurt (Svenska Sockerfabriks AB, Swed.). Eur. Pat. Appl. EP 226563 A1 19870624, 18 pp. DESIGNATED STATES: R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1986-850414 19861202. PRIORITY: SE 1985-5842 19851211.

AB A method for controlling the regioselectivity of the glycosidic bond formed glycosyl donor and glycosyl acceptor in the enzymic production of an oligosaccharide compound, which either consists of or is a fragment or an analog of the carbohydrate part in a **glycoconjugate**, by reverse hydrolysis or transglycosidation is described. The method also facilitates purification of the products and facilitates their use in preparation of **glycoconjugates** (e.g. glycoproteins, glycolipids) which may be used for drug **targeting** or for diagnosis and treatment of diseases, e.g. cancer. Methyl-3-O-α-D-galactopyranosyl-α-D-galactopyranoside was prepared in 39% yield by the action of coffee bean α-galactosidase (EC 3.2.1.22) on Gal(α-O-p-nitrophenyl and Gal(α)-OMe in an aqueous solution of Na **phosphate** (pH 6.5) and N,N-dimethylformamide.

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=> s l18 and phosphinate
L27          0 L18 AND PHOSPHINATE

=> s l18 and sulfate
L28          1 L18 AND SULFATE

=> d l28 cbib abs

L28  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2008 ACS on STN
2005:122585   Document No. 142:217398  Cell-free in vitro glycoconjugation of
     interleukin 2 as therapeutic agent against cancer and AIDS in mammal and
     human.  Defrees, Shawn; Zopf, David; Bayer, Robert; Bowe, Caryn; Hakes,
     David; Chen, Xi (Neose Technologies, Inc., USA).  U.S. Pat. Appl. Publ. US
     20050031584 A1 20050210, 750 pp., Cont.-in-part of U.S. Ser. No. 360,779.
     (English).  CODEN: USXXCO.  APPLICATION: US 2003-410980 20030409.
     PRIORITY: US 2001-328523P 20011010; US 2001-344692P 20011019; US
     2001-334301P 20011128; US 2001-334233P 20011128; US 2002-387292P 20020607;
     US 2002-391777P 20020625; US 2002-396594P 20020717; US 2002-404249P
     20020816; US 2002-407527P 20020828; WO 2002-US32263 20021009; US
     2002-287994 20021105; US 2003-360770 20030106; US 2003-360779 20030219.
AB   The invention includes methods and compns. for remodeling a peptide mol.,
     including the addition or deletion of one or more glycosyl groups to a
     peptide, and/or the addition of a modifying group to a peptide.  The method
     uses enzyme to remove or add phosphate, sulfate, carboxylate
     and/or ester group-containing saccharide to interleukin 2 peptide, and then
     conjugate the saccharide-linked interleukin 2 with modifying group such as
     polymer, therapeutic moiety, detectable label, toxin, radioisotope,
     targeting moiety and peptide.  The saccharide group comprises
     monosaccharyl, oligosaccharyl, glycosyl, truncated glycan, mannosyl,
     GlcNAc, xylosyl, sialyl, galactosyl, glucosyl or GalNAc.  The enzyme for
     the saccharide addition or removal is a prokaryotic or eukaryotic
     glycosyltransferase selected from sialyltransferase,
     galactosyltransferase, glucosyltransferase, GalNAc transferase, GlcNAc
     transferase, fucosyltransferase, mannosyltransferase,
     endo-N-acetylgalactosaminidase, glycosidase, sialidase, mannosidase, etc.
     The substrate is a nucleotide sugar such as UDP-glucose, UDP-
     galactose, UDP-galactosamine, UDP-glucosamine,
     UDP-N-acetylgalactosamine, UDP-N-acetylglucosamine, GDP-mannose,
     GDP-fucose, CMP-sialic acid and CMP-NeuAc.


=> s l18 and sulfinate
L29          0 L18 AND SULFINATE

=> s (qasba p?/au or ramakrishnan b?/au)
L30        866 (QASBA P?/AU OR RAMAKRISHNAN B?/AU)

=> s l30 and glycoconjugate?
L31         35 L30 AND GLYCOCONJUGATE?

=> s l31 and target?
L32         14 L31 AND TARGET?

=> dup remove l32
PROCESSING COMPLETED FOR L32
L33           9 DUP REMOVE L32 (5 DUPLICATES REMOVED)

=> d l33 1-9 cbib abs

L33  ANSWER 1 OF 9     MEDLINE on STN                    DUPLICATE 1
2008368926.    PubMed ID: 18426242.   Site-specific linking of biomolecules via
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glycan residues using glycosyltransferases. **Qasba Pradman K**; Boeggeman Elizabeth; **Ramakrishnan Boopathy**. (Structural Glycobiology Section, SAIC-Frederick, Inc., Center for Cancer Research Nanobiology Program, Center for Cancer Research, NCI-Frederick, Frederick, Maryland 21702, USA.. qasba@helix.nih.gov) . Biotechnology progress, (2008 May-Jun) Vol. 24, No. 3, pp. 520-6. Electronic Publication: 2008-04-22. Journal code: 8506292. E-ISSN: 1520-6033. Pub. country: United States. Language: English.

AB The structural information on glycosyltransferases has revealed that the sugar-donor specificity of these enzymes can be broadened to include modified sugars with a chemical handle that can be utilized for conjugation chemistry. Substitution of Tyr289 to Leu in the catalytic pocket of bovine beta-1,4-galactosyltransferase generates a novel glycosyltransferase that can transfer not only Gal but also GalNAc or a C2-modified galactose that has a chemical handle, from the corresponding UDP-derivatives, to the non-reducing end GlcNAc residue of a **glycoconjugate**. Similarly, the wild-type polypeptide-N-acetyl-galactosaminyltransferase, which naturally transfers GalNAc from UDP-GalNAc, can also transfer C2-modified galactose with a chemical handle from its UDP-derivative to the Ser/Thr residue of a polypeptide acceptor substrate that is tagged as a fusion peptide to a non-glycoprotein. The potential of wild-type and mutant glycosyltransferases to produce **glycoconjugates** carrying sugar moieties with chemical handle makes it possible to conjugate biomolecules with orthogonal reacting groups at specific sites. This methodology assists in the assembly of bio-nanoparticles that are useful for developing **targeted** drug-delivery systems and contrast agents for magnetic resonance imaging.

L33 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN

2008:390303 New synthetic sugar-nucleotide donor substrates for glycosyltransferases. Manzoni, Maria R.; Boeggeman, Elizabeth; **Ramakrishnan, Boopathy**; Pasek, Marta; **Qasba, Pradman Krishen** (Structural Glycobiology Section, Nanobiology Program, Center for Cancer Research, National Cancer Institute-NIH, Frederick, MD, 21702-1201, USA). Abstracts of Papers, 235th ACS National Meeting, New Orleans, LA, United States, April 6-10, 2008, ORGN-275. American Chemical Society: Washington, D. C. (English) 2008. CODEN: 69KNN3.

AB Considering the important role of **glycoconjugates** in biol. recognition, acute and chronic diseases (such as inflammation), and numerous cancer types; methods capable of introducing a sugar residue with a reactive chemical handle at a unique site in the oligosaccharide chain of relevant glycoprotein and/or glycolipid are highly desirable. Structure-based design of novel glycosyltransferases is making it possible to transfer unnatural sugars to specific monosaccharide residue on a glycan chain. These carbohydrates with chemical handles have been shown to be new sugar-donor substrates for natural and engineered mutant glycosyltransferases. While exploiting this selective, chemoenzymic approach, these functionalized, unnatural **glycoconjugates** have a variety of new diagnostic and therapeutic applications allowing for the incorporation of probes, biomarkers, and/or drug-**targeting** systems.

L33 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN

2008:950006 Useful applications of synthetic modified-sugar nucleotide donor substrates. Manzoni, Maria R.; Boeggeman, Elizabeth; **Ramakrishnan, Boopathy; Qasba, Pradman Krishen** (Structural Glycobiology Section, Nanobiology Program, Center for Cancer Research, National Cancer Institute-NIH, Frederick, MD, 21702-1201, USA). Abstracts of Papers, 236th ACS National Meeting, Philadelphia, PA, United States, August 17-21, 2008, BIOT-167. American Chemical Society: Washington, D. C. (English) 2008. CODEN: 69KXQ2.

AB Considering the important role of **glycoconjugates** in biol. recognition, acute and chronic diseases (such as inflammation), and numerous cancer types; methods capable of introducing a sugar residue with a reactive chemical handle at a unique site in the oligosaccharide chain of relevant glycoprotein and/or glycolipid are highly desirable. Structure-based design of novel glycosyltransferases is making it possible to transfer unnatural sugars to a specific monosaccharide residue on a glycan chain or directly to a peptide because these carbohydrates with chemical handles have been shown to be new sugar-donor substrates for natural and engineered mutant glycosyltransferases. While exploiting this selective, chemoenzymic approach, these functionalized, unnatural **glycoconjugates** have a variety of new diagnostic and therapeutic applications allowing for the incorporation of probes, biomarkers, and development of drug-**targeting** systems. We are currently synthesizing novel unnatural carbohydrates that will contain the functionality for incorporating probes and/or biomarkers; namely, we plan to exploit this technol. for the anal. of "over-" and "under-" glycosylated glycans related to certain disease. These techniques will facilitate the diagnosis of a diseases by tracing of aberrant glycosylation patterns associated with the diseases, as well as the anal. of specific **glycoconjugates** related to biol. recognition. The usefulness of this conjugation method will be discussed since we have developed mutant glycosyltransferases that are capable of transferring modified sugars to specific monosaccharide residue of therapeutic monoclonal antibodies in a selective, controlled manner. Thus, this technol. is also applicable to drug development.

L33 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
2007:321112 Document No. 146:517239 Direct Identification of Nonreducing GlcNAc Residues on N-Glycans of Glycoproteins Using a Novel Chemoenzymatic Method. Boeggeman, Elizabeth; **Ramakrishnan, Boopathy**; Kilgore, Charlton; Khidekel, Nelly; Hsieh-Wilson, Linda C.; Simpson, John T.; **Qasba, Pradman K.** (Structural Glycobiology Section, CCR-Nanobiology Program, Center for Cancer Research, NCI-Frederick, Frederick, MD, 21702, USA). Bioconjugate Chemistry, 18(3), 806-814 (English) 2007. CODEN: BCCHES. ISSN: 1043-1802. Publisher: American Chemical Society.
AB The mutant β1,4-galactosyltransferase (β4Gal-T1), β4Gal-T1-Y289L, in contrast to wild-type β4Gal-T1, can transfer GalNAc from the sugar donor UDP-GalNAc to the acceptor, GlcNAc, with efficiency as good as that of galactose from UDP-Gal. Furthermore, the mutant can also transfer a modified sugar, C2 keto galactose, from its UDP derivative to O-GlcNAc modification on proteins that provided a functional handle for developing a highly sensitive chemoenzymic method for detecting O-GlcNAc post-translational modification on proteins. We report herein that the modified sugar, C2 keto galactose, can be transferred to free GlcNAc residues on N-linked glycoproteins, such as ovalbumin or asialo-agalacto IgG1. The transfer is strictly dependent on the presence of both the mutant enzyme and the ketone derivative of the galactose. Moreover, the PNGase F treatment of the glycoproteins, which cleaves the N-linked oligosaccharide chain, shows that the modified sugar has been transferred to the N-glycan chains of the glycoproteins and not to the protein portion. The application of the mutant galactosyltransferase, β4Gal-T1-Y289L, to produce **glycoconjugates** carrying sugar moieties with reactive groups, is demonstrated. We envision a broad potential for this technol. such as the possibilities to link cargo mols. to glycoproteins, such as monoclonal antibodies, via glycan chains, thereby assisting in the glyco-**targeting** of drugs to the site of action or used as biol. probes.

L33 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
2007:879157 Mutant glycosyltransferases assist in linking

glycoconjugates via glycan chains: Development of a **targeted** drug delivery system and contrast agents for MRI. **Qasba, Pradman Krishen**; Boeggeman, Elizabeth; **Ramakrishnan, Boopathy** (Structural Glycobiology Section, Nanobiology Program, Center for Cancer Research, NCI-Frederick, NCI, NIH, Frederick, MD, 21702-1203, USA). Abstracts of Papers, 234th ACS National Meeting, Boston, MA, United States, August 19-23, 2007, BIOT-185. American Chemical Society: Washington, D. C. (English) 2007. CODEN: 69JNR2.

AB The structural information of glycosyltransferases has revealed that the specificity of the sugar donor in these enzymes is determined by a few residues in the sugar-nucleotide binding pocket of the enzyme, conserved among the family members from different species. This in turn has made it possible to reengineer the existing glycosyltransferases with broader sugar donor specificities. Mutation of these residues generates novel glycosyltransferases that can transfer a sugar residue with a chemical reactive functional group to N-acetylglucosamine (GlcNAc), galactose (Gal) and xylose residues of glycoproteins, glycolipids and proteoglycans (**glycoconjugates**). The potential of mutant glycosyltransferases to produce **glycoconjugates** carrying sugar moieties with reactive groups which can be used subsequently in the assembly of bio-nanoparticles is making it possible to develop a **targeted**-drug delivery system and contrast agents for MRI. This project has been funded in whole or in part with federal funds from the NCI, National Institutes of Health, under contract N01-CO-12400.

L33 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN

2007:520558 Syntheses of unnatural **glycoconjugates** with vast biological applications. Manzoni, Maria R.; **Ramakrishnan, Boopathy**; Boeggeman, Elizabeth; **Qasba, Pradman K.** (Center for Cancer Research-Nanobiology Program, National Cancer Institutute-NIH, Frederick, MD, 21702, USA). Abstracts, 39th Middle Atlantic Regional Meeting of the American Chemical Society, Collegeville, PA, United States, May 16-18, MARM-129. American Chemical Society: Washington, D. C. (English) 2007. CODEN: 69JFDW.

AB In view of the important role of **glycoconjugates** in biol. recognition, acute and chronic diseases (such as inflammation), and numerous cancer types; methods capable of introducing an unnatural sugar at a unique site in the oligosaccharide chain of relevant glycoprotein and/or glycolipid are highly desirable. We have developed mutant glycosyltransferases that are capable of transferring modified sugars to specific monosaccharide residue on a glycan chain. We are currently synthesizing novel unnatural carbohydrates that will contain the functionality for incorporating probes and/or biomarkers. We plan to exploit this technol. for the anal. of "under-" and "over-glycosylated" glycans related to certain disease. These techniques will facilitate the tracing of aberrant glycosylation patterns associated with diseases, as well as the anal. or diagnosis of specific **glycoconjugates** related to biol. recognition, and drug therapy. In addition, this method may have vast biol. applications, such as the development of **targeted** drug delivery systems, fluorescent derivitization for glycomic anal., or contrast agents for MRI.

L33 ANSWER 7 OF 9 MEDLINE on STN DUPLICATE 2

2006186546. PubMed ID: 16584127. Mutant glycosyltransferases assist in the development of a **targeted** drug delivery system and contrast agents for MRI. **Qasba Pradman K; Ramakrishnan Boopathy** ; Boeggeman Elizabeth. (Structural Glycobiology Section, Nanobiology Program, CCR, NCI-Frederick, Frederick, MD, USA.. qasba@helix.nih.gov) . The AAPS journal, (2006) Vol. 8, No. 1, pp. E190-5. Electronic Publication: 2006-03-24. Ref: 64. Journal code: 101223209. E-ISSN: 1550-7416. Pub. country: United States. Language: English.

AB The availability of structural information on glycosyltransferases is

beginning to make structure-based reengineering of these enzymes possible. Mutant glycosyltransferases have been generated that can transfer a sugar residue with a chemically reactive unique functional group to a sugar moiety of glycoproteins, glycolipids, and proteoglycans (**glycoconjugates**). The presence of modified sugar moiety on a glycoprotein makes it possible to link bioactive molecules via modified glycan chains, thereby assisting in the assembly of bionanoparticles that are useful for developing the **targeted** drug delivery system and contrast agents for magnetic resonance imaging. The reengineered recombinant glycosyltransferases also make it possible to (1) remodel the oligosaccharide chains of glycoprotein drugs, and (2) synthesize oligosaccharides for vaccine development.

L33 ANSWER 8 OF 9 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN

2006159419 EMBASE Mutant glycosyltransferases assist in the development of a **targeted** drug delivery system and contrast agents for MRI.

Qasba, Pradman K. (correspondence); Ramakrishnan, Boopathy; Boeggeman, Elizabeth. Structural Glycobiology Section, Nanobiology Program, NCI-Frederick, Building 469, Frederick, MD 21702, United States. qasba@helix.nih.gov. **Ramakrishnan, Boopathy**; Boeggeman, Elizabeth. Basic Research Program, SAIC-Frederick Inc., Frederick, MD, United States. **Qasba, Pradman K. (correspondence)** . Structural Glycobiology Section, CCRNP, NCI-Frederick, Building 469, Frederick, MD 21702, United States. qasba@helix.nih.gov.

AAPS Journal Vol. 8, No. 1, pp. E190-E195 24 Mar 2006. arn. 23

Refs: 64.

ISSN: 1550-7416.

Pub. Country: United States. Language: English. Summary Language: English.

Entered STN: 20060412. Last Updated on STN: 20060412

AB The availability of structural information on glycosyltransferases is beginning to make structure-based reengineering of these enzymes possible. Mutant glycosyltransferases have been generated that can transfer a sugar residue with a chemically reactive unique functional group to a sugar moiety of glycoproteins, glycolipids, and proteoglycans (**glycoconjugates**). The presence of modified sugar moiety on a glycoprotein makes it possible to link bioactive molecules via modified glycan chains, thereby assisting in the assembly of bionanoparticles that are useful for developing the **targeted** drug delivery system and contrast agents for magnetic resonance imaging. The reengineered recombinant glycosyltransferases also make it possible to (1) remodel the oligosaccharide chains of glycoprotein drugs, and (2) synthesize oligosaccharides for vaccine development.

L33 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN

2005:490304 Document No. 143:48058 **Targeted** delivery system for bioactive agents. **Qasba, Pradman; Ramakrishnan, Boopathy** (ushu, USA). PCT Int. Appl. WO 2005051429 A2 20050609, 63 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IS, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-US38781 20041118. PRIORITY: US 2003-523112P 20031119.

AB In accordance with the present invention, compds., compns. and methods are provided that allow for the administration of a bioactive agent to an organism, including a human or an animal. The present invention can be

used to treat or prevent a disease and/or disorder with a bioactive agent, or can be used to safely vaccinate a human or animal against a bioactive agent. The invention can also be used as a method for the delivery of bioactive agents for the treatment or prevention of a disease and/or a disorder, particularly **targeted** delivery of bioactive agents through the administration of **glycoconjugates** containing a bioactive agent bound to a **targeting** compound through a modified saccharide residue. A chemoenzymic approach toward the rapid and sensitive detection of O-GlcNAc posttranslational modifications is also described.

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=> s glycoconjugate
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L1       32355 GLYCOCONJUGATE

=> s l1 and chemoenzymatic
L2         141 L1 AND CHEMOENZYMATIC

=> s l2 and 2-keto-Gal
L3           0 L2 AND 2-KETO-GAL

=> s l1 and 2-keto-Gal
L4           0 L1 AND 2-KETO-GAL

=> s l2 and galactosyltransferase
L5          14 L2 AND GALACTOSYLTRANSFERASE

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L6            6 DUP REMOVE L5 (8 DUPLICATES REMOVED)

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L6   ANSWER 1 OF 6     MEDLINE on STN                    DUPLICATE 1
2007347589.    PubMed ID: 17370997.   Direct identification of nonreducing
     GlcNAc residues on N-glycans of glycoproteins using a novel
     chemoenzymatic method. Boeggeman Elizabeth; Ramakrishnan Boopathy;
     Kilgore Charlton; Khidekel Nelly; Hsieh-Wilson Linda C; Simpson John T;
     Qasba Pradman K. (Structural Glycobiology Section, CCR-Nanobiology
     Program, Center for Cancer Research, NCI-Frederick, Frederick, Maryland
     21702, USA. ) Bioconjugate chemistry, (2007 May-Jun) Vol. 18, No. 3, pp.
     806-14.  Electronic Publication: 2007-03-20. Journal code: 9010319. ISSN:
     1043-1802. Pub. country: United States. Language: English.
AB   The mutant beta1,4-galactosyltransferase (beta4Gal-T1),
     beta4Gal-T1-Y289L, in contrast to wild-type beta4Gal-T1, can transfer
     GalNAc from the sugar donor UDP-GalNAc to the acceptor, GlcNAc, with
     efficiency as good as that of galactose from UDP-Gal.  Furthermore, the
     mutant can also transfer a modified sugar, C2 keto galactose, from its UDP
     derivative to O-GlcNAc modification on proteins that provided a functional
     handle for developing a highly sensitive chemoenzymatic method
     for detecting O-GlcNAc post-translational modification on proteins.  We
     report herein that the modified sugar, C2 keto galactose, can be
     transferred to free GlcNAc residues on N-linked glycoproteins, such as
     ovalbumin or asialo-agalacto IgG1.  The transfer is strictly dependent on
     the presence of both the mutant enzyme and the ketone derivative of the
     galactose.  Moreover, the PNGase F treatment of the glycoproteins, which
     cleaves the N-linked oligosaccharide chain, shows that the modified sugar
     has been transferred to the N-glycan chains of the glycoproteins and not
     to the protein portion.  The application of the mutant
     galactosyltransferase, beta4Gal-T1-Y289L, to produce
     glycoconjugates carrying sugar moieties with reactive groups, is
     demonstrated.  We envision a broad potential for this technology such as
     the possibilities to link cargo molecules to glycoproteins, such as
     monoclonal antibodies, via glycan chains, thereby assisting in the
     glycotargeting of drugs to the site of action or used as biological
     probes.

L6   ANSWER 2 OF 6  CAPLUS  COPYRIGHT 2009 ACS on STN
2003:939066   Document No. 140:1116260  Chemoenzymatic Synthesis and
     Antibody Detection of DNA Glycoconjugates.  Wang, Yingli;
     Sheppard, Terry L. (Department of Chemistry and The Robert H. Lurie
     Comprehensive Cancer Center, Northwestern University, Evanston, IL,
     60208-3113, USA).  Bioconjugate Chemistry, 14(6), 1314-1322 (English)
     2003.  CODEN: BCCHES.  ISSN: 1043-1802.  OTHER SOURCES: CASREACT
     140:111626.  Publisher: American Chemical Society.
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AB A chemoenzymic approach for the efficient synthesis of DNA-carbohydrate conjugates was developed and applied to an antibody-based strategy for the detection of DNA **glycoconjugates.** A phosphoramidite derivative of N-acetylglucosamine (GlcNAc) was synthesized and utilized to attach GlcNAc sugars to the 5'-terminus of DNA oligonucleotides by solid-phase DNA synthesis. The resulting GlcNAc-DNA conjugates were used as substrates for glycosyl transferase enzymes to synthesize DNA **glycoconjugates** . Treatment of GlcNAc-DNA with β-1,4-galactosyl transferase (GalT) and UDP-Gal produced N-acetyllactosamine-modified DNA (LacNAc-DNA), which could be converted quant. to the trisaccharide Lewis X (LeX)-DNA conjugate by α-1,3-fucosyltransferase VI (FucT) and GDP-Fuc. The facile enzymic synthesis of LeX-DNA from GlcNAc-DNA also was accomplished in a one-pot reaction by the combined action of GalT and FucT. The resulting **glycoconjugates** were characterized by gel electrophoresis, matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS), and glycosidase digestion expts. Covalent modification of the 5'-terminus of DNA with carbohydrates did not interfere with the ability of DNA **glycoconjugates** to hybridize with complementary DNA, as indicated by UV thermal denaturation anal. The trisaccharide DNA **glycoconjugate**, LeX-DNA, was detected by a dual DNA hybridization/monoclonal antibody (mAb) detection protocol ("Southwestern"): membrane-immobilized LeX-DNA was visualized by Southern detection with a radiolabeled complementary DNA probe and by Western chemiluminescence detection with a mAb specific for the LeX antigen. The efficient chemoenzymic synthesis of DNA **glycoconjugates** and the Southwestern detection protocol may facilitate the application of glycosylated DNA to cellular targeting and DNA **glycoconjugate** detection strategies.

L6 ANSWER 3 OF 6 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN

2001:339747 The Genuine Article (R) Number: 421UK. Specificity and mechanism of metal ion activation in UDP-galactose :beta-Galactoside-alpha-1,3-**galactosyltransferase.**

Brew K (Reprint). Florida Atlantic Univ, Dept Biomed Sci, 777 Glades Rd, Boca Raton, FL 33431 USA (Reprint). Zhang Y N; Wang P G. Univ Miami, Sch Med, Dept Biochem & Mol Biol, Miami, FL 33101 USA; Wayne State Univ, Dept Chem, Detroit, MI 48202 USA.

JOURNAL OF BIOLOGICAL CHEMISTRY (13 APR 2001) Vol. 276, No. 15, pp. 11567-11574. ISSN: 0021-9258. Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814 USA. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB UDP-galactose:beta -galactosyl-alpha1,3-**galactosyltransferase** (alpha 3GT) catalyzes the synthesis of galactosyl-alpha -1,3-beta -galactosyl structures in mammalian **glycoconjugates.** In humans the gene for a3GT is inactivated, and its product, the alpha -Gal epitope, is the target of a large fraction of natural antibodies. alpha 3GT is a member of a family of metal-dependent-retaining glycosyltransferases that includes the histo blood group A and B enzymes. Mn2+ activates the catalytic domain of alpha 3GT (alpha 3GTcd), but the affinity reported for this ion is very low relative to physiological levels. Enzyme activity over a wide range of metal ion concentrations indicates a dependence on Mn2+ binding to two sites. At physiological metal ion concentrations, Zn2+ gives higher levels of activity and may be the natural cofactor. To determine the role of the cation, metal activation was perturbed by substituting Co2+ and Zn2+ for Mn2+ and by mutagenesis of a conserved (DVD151)-V-149 sequence motif that is considered to act in cation binding in many glycosyltransferases. The aspartates of this motif were found to be essential for activity, and the kinetic properties of a Val(150) to Ala mutant with reduced activity were determined. The results indicate that the cofactor is involved in binding UDP-galactose and has a crucial

influence on catalytic efficiency for galactose transfer and for the low endogenous UDP-galactose hydrolase activity. It may therefore interact with one or more phosphates of UDP-galactose in the Michaelis complex and in the transition state for cleavage of the UDP to galactose bond. The DXD motif conserved in many glycosyltransferases appears to have a key role in metal-mediated donor substrate binding and phosphate-sugar bond cleavage.

L6 ANSWER 4 OF 6 MEDLINE on STN DUPLICATE 2

2002210359. PubMed ID: 11948877. **Chemoenzymatic** synthesis of biotinylated nucleotide sugars as substrates for glycosyltransferases. Bulter T; Schumacher T; Namdjou D J; Gutierrez Gallego R; Clausen H; Elling L. (Institute of Enzyme Technology, Heinrich-Heine University of Dusseldorf, Research Center Julich, 52426 Julich, Germany.) Chembiochem : a European journal of chemical biology, (2001 Dec 3) Vol. 2, No. 12, pp. 884-94. Journal code: 100937360. ISSN: 1439-4227. Pub. country: Germany: Germany, Federal Republic of. Language: English.

AB The enzymatic oxidation of uridine 5'-diphospho-alpha-D-galactose (UDP-Gal) and uridine 5'-diphospho-N-acetyl-alpha-D-galactosamine (UDP-GalNAc) with galactose oxidase was combined with a chemical biotinylation step involving biotin-epsilon-amidocaproylhydrazide in a one-pot synthesis. The novel nucleotide sugar derivatives uridine 5'-diphospho-6-biotin-epsilon-amidocaproylhydrazino-alpha-D-galactose (UDP-6-biotinyl-Gal) and uridine 5'-diphospho-6-biotin-epsilon-amidocaproylhydrazino-N-acetyl-alpha-D-galactosamine (UDP-6-biotinyl-GalNAc) were synthesized on a 100-mg scale and characterized by mass spectrometry (fast atom bombardment and matrix-assisted laser desorption/ionization time of flight) and one/two dimensional NMR spectroscopy. It could be demonstrated for the first time, by use of UDP-6-biotinyl-Gal as a donor substrate, that the human recombinant **galactosyltransferases** beta3Gal-T5, beta4Gal-T1, and beta4Gal-T4 mediate biotinylation of the neoglycoconjugate bovine serum albumin-p-aminophenyl N-acetyl-beta-D-glucosaminide (BSA-(GlcNAc)17) and ovalbumin. The detection of the biotin tag transferred by beta3Gal-T5 onto BSA-(GlcNAc)17 with streptavidin-enzyme conjugates gave detection limits of 150 pmol of tagged GlcNAc in a Western blot analysis and 1 pmol of tagged GlcNAc in a microtiter plate assay. The degree of Gal-biotin tag transfer onto agalactosylated hybrid N-glycans present at the single glycosylation site of ovalbumin was dependent on the Gal-T used (either beta3Gal-T5, beta4Gal-T4, or beta4Gal-T1), which indicates that the acceptor specificity may direct the transfer of the Gal-biotin tag. The potential of this biotinylated UDP-Gal as a novel donor substrate for human **galactosyltransferases** lies in the targeting of distinct acceptor structures, for example, under-galactosylated **glycoconjugates**, which are related to diseases, or in the quality control of glycosylation of recombinant and native glycoproteins.

L6 ANSWER 5 OF 6 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN

1999:629343 The Genuine Article (R) Number: 228LG. Bacteria targeted by human natural antibodies using alpha-Gal conjugated receptor-specific glycopolymers.

Wang P G (Reprint). Wayne State Univ, Dept Chem, Detroit, MI 48202 USA (Reprint). Li J; Zacharek S; Chen X; Wang J Q; Zhang W; Janczuk A. BIOORGANIC & MEDICINAL CHEMISTRY (AUG 1999) Vol. 7, No. 8, pp. 1549-1558. ISSN: 0968-0896. Publisher: PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, ENGLAND. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Synthesis of polymerizable beta-lactosyl, Gal alpha 1-->3Gal and alpha-mannosyl acrylamide derivatives with either a hydrophobic aromatic spacer or a hydrophilic biocompatible oligoethoxyl spacer was accomplished. Radical terpolymerizations of beta-lactosyl monomer,

alpha-mannosyl monomer, and acrylamide were conducted in aqueous media with ammonium persulfate and N,N,N,N'-tetramethylethylenediamine as initiators. The resulting water soluble glycopolymers were further transformed efficiently by a recombinant alpha 1-->3 **galactosyltransferase** to afford mediators bearing Gal alpha 1-->3Gal termini as xenoactive antigens and alpha-mannosyl termini as specific ligands for bacterial cells. The binding of the resulting multivalent glycopolymer to bacteria was tested by its ability to inhibit agglutination of yeast to E. coli. The binding of human natural anti-Gal antibodies to the alpha-Gal containing glycopolymers and a monovalent alpha-Gal-Man **glycoconjugate** was demonstrated by an ELISA inhibition assay.

L6 ANSWER 6 OF 6 MEDLINE on STN DUPLICATE 3
1996415269. PubMed ID: 8818236. Ergot alkaloid glycosides with immunomodulatory activities. Kren V; Fiserova A; Auge C; Sedmera P; Havlicek V; Sima P. (Institute of Microbiology, Academy of Sciences of the Czech Republic, Prague, Czech Republic.) Bioorganic & medicinal chemistry, (1996 Jun) Vol. 4, No. 6, pp. 869-76. Journal code: 9413298. ISSN: 0968-0896. Pub. country: ENGLAND: United Kingdom. Language: English.
AB New glycosides derived from ergot alkaloids elymoclavine and DH-lysergol were synthesized by **chemoenzymatic** methods. beta-Glucosides were obtained either by chemical method or by transglycosylation (glycosidase from Aspergillus oryzae), lactosides were prepared by further extension of carbohydrate chain using beta-1,4-**galactosyltransferase** (bovine milk) and alpha-5-N-acetylneuraminyl-(2-->6)-beta-D-galactopyranosyl-(1-->4)-2- acetamido-2-deoxy-beta-D-glucopyranosyl-(1-->O)-elymoclavine was prepared using alpha-2,6-sialyltransferase (rat liver). Immunomodulatory activity of elymoclavine and 9,10-dihydrolysergol and their glycosylated derivatives on natural killer (NK) cell-mediated cytotoxicity of human resting and activated human peripheral blood mononuclear cells (PBMC) was investigated. Addition of ergot alkaloid glycosides to the mixtures of effector and target cells potentiated the PBMC cytotoxicity against both NK-sensitive and -resistant target cells. The **glycoconjugates** of elymoclavine enhanced cytotoxicity of PBMC against NK-resistant target cells. The **glycoconjugates** of DH-lysergol potentiated NK cytotoxicity of PBMC against NK-sensitive target cells.

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L7         125 L1 AND C2

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L8          50 L7 AND GALACTOSE

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L9          28 L8 AND PD<20031119

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L10           9 DUP REMOVE L9 (19 DUPLICATES REMOVED)

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L10 ANSWER 1 OF 9 MEDLINE on STN DUPLICATE 1
2003177267. PubMed ID: 12695119. Dextran-binding human plasma antibody recognizes bacterial and yeast antigens and is inhibited by glucose concentrations reached in diabetic sera. Chacko B K; Appukuttan P S. (Division of Biochemistry, Sree Chitra Tirunal Institute for Medical Sciences and Technology, 695011, Thiruvananthapuram, India.) Molecular immunology, **(2003 May)** Vol. 39, No. 15, pp. 933-9. Journal

code: 7905289. ISSN: 0161-5890. Pub. country: England: United Kingdom. Language: English.

AB Dextran-binding antibody was isolated in high yield from plasma of all 40 blood donors screened in a South Indian population. The antibody was purified by a single step affinity chromatography on Sephadex G100 using 1-O-methyl alpha-D-glucoside as eluant. Analysis of protein peaks obtained in size exclusion high pressure liquid chromatography (HPLC) revealed dominance of IgG and suggested the presence of polymeric IgA in this antibody. Methyl and para-nitrophenyl alpha-D-glucosides, in contrast to their beta-anomers, were very efficient inhibitors of binding of this antibody to dextran. **Galactose** and glucose were equally good inhibitors. Among disaccharide inhibitors sucrose was more efficient than maltose or melibiose. Hemoglobin artificially glycosylated to contain covalently-linked glucose or alpha-anomeric **galactose** was sugar-specifically recognized by this antibody. **Galactose** moieties in glycoproteins or polysaccharides were, however, not recognized. The dextran-binding antibody bound sugar-specifically to **glycoconjugates** from yeast (Saccharomyces cerevisiae) and to lipopolysaccharides from Klebsiella and group A Streptococci, but not to lipopolysaccharides from E. coli. Inhibition studies suggested glucose moiety with unsubstituted **C2** and C4 and alpha-anomeric C1 as ideal for recognition by the dextran-binding antibody. Concentration of glucose required for 50% inhibition of binding of the purified antibody to polystyrene-coated dextran in phosphate buffered saline was above the glucose concentrations in normal sera, but well below those reached in diabetic sera. Binding of the antibody from dialysed plasma to immobilized dextran was lowered only marginally in presence of glucose at 4.5mM (which nears normal serum glucose concentrations), but substantially in presence of the sugar at 20mM and above which are reached in diabetic sera. If verified in vivo, inhibition of this antibody by high serum glucose may possibly be among reasons for the increased susceptibility of diabetics to infection.

L10 ANSWER 2 OF 9 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

2003:37060 Document No.: PREV200300037060. Self-assembled monolayers of globotriaosylceramide (Gb3) mimics: Surface-specific affinity with Shiga toxins. Miura, Yoshiko [Reprint Author]; Sasao, Yuuki; Dohi, Hirofumi; Nishida, Yoshihiro; Kobayashi, Kazukiyo. Department of Molecular Design and Engineering, Graduate School of Engineering, Nagoya University, Furo-cho, Chikusa-ku, Nagoya, 464-8603, Japan. miuray@mol.nagoya-u.ac.jp. Analytical Biochemistry, (**November 1 2002**) Vol. 310, No. 1, pp. 27-35. print.
ISSN: 0003-2697 (ISSN print). Language: English.

AB Self-assembled monolayers (SAMS) of Gb3 mimics having different lengths of alkyl chains were prepared on gold surfaces, and their interactions with **galactose**-specific lectin (RCA120) and Shiga toxins (Stxs) were investigated by a quartz crystal microbalance (QCM) in aqueous solutions. Their interaction with RCA120 was enhanced owing to the "cluster effect," regardless of the alkyl chain length of the SAMs. The interaction with Stxs was dependent on the alkyl chain length of Gb3 mimics. Stx-1 and Stx-2 showed a stronger affinity to the Gb3C2 SAM with ethyl disulfide and to the Gb3C10 with decyl disulfide, respectively. Gb3 **glycoconjugate** polymer with no alkyl spacer inhibited the adsorption of Stx-1 to Gb3C10 SAM but did not inhibit the adsorption of Stx-2 to Gb3C10 SAM. The results suggest that the alkyl chain of the glycolipid takes part in the binding to Stx-2 but not to Stx-1, which is also supported by the computer simulation of Stx-1 with a Gb3 model substance.

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2003456989 EMBASE α2,3-sialylation of terminal GalNAcβ1-3Gal

determinants by ST3Gal II reveals the multifunctionality of the enzyme: The resulting Neu5acα2-3GalNac linkage is resistant to sialidases from newcastle disease virus and Streptococcus pneumoniae.
Toivonen, Suvi; Aitio, Olli; Renkonen, Ossi (correspondence). Institute of Biotechnology, Department of Biosciences, University of Helsinki, 00014 Helsinki, Finland. ossi.renkonen@helsinki.fi. Aitio, Olli. Viikki Drug Discov. Technol. Center, Department of Pharmacy, University of Helsinki, 00014 Helsinki, Finland. Renkonen, Ossi (correspondence). Biomedicum Helsinki, University of Helsinki, P. O. Box 63, 00014 Helsinki, Finland. ossi.renkonen@helsinki.fi.
Journal of Biological Chemistry Vol. 276, No. 40, pp. 37141-37148 **5 Oct 2001.**
Refs: 57.
ISSN: 0021-9258. CODEN: JBCHA3.
Pub. Country: United States. Language: English. Summary Language: English.
Entered STN: 20031211. Last Updated on STN: 20031211

AB Enzymatic α2,3-sialylation of GalNAc has not been described previously, although some **glycoconjugates** containing α2,3-sialylated GalNAc residues have been reported. In the present experiments, recombinant soluble α2,3-sialyltransferase ST3Gal II efficiently sialylated the X (2) pentasaccharide GalNAcβ1-3Galβ1-4GlcNAcβ1-3Galβ 1-4Glc, globo-N-tetraose GalNAcβ1-3Galα1-4Galβ1-4Glc, and the disaccharide GalNAβ1-3Gal in vitro. The purified products were identified as Neu5Acα2-3GalNAcβ1-3Galβ1-4GlcNAcβ1-3Galβ1-4Glc, Neu5Acα2-3GalNAcβ1-3Galα1-4Galβ1-4Glc, and Neu5Acα2-3GalNAcβ1-3Gal, respectively, by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry, enzymatic degradations, and one- and two-dimensional NMR-spectroscopy. In particular, the presence of the Neu5Acα2-3GalNAc linkage was firmly established in all three products by a long range correlation between Neu5Ac **C2** and GalNAc H3 in heteronuclear multiple bond correlation spectra. Collectively, the data describe the first successful sialyltransfer reactions to the 3-position of GalNAc in any acceptor. Previously, ST3Gal II has been shown to transfer to the Galβ1-3GalNAc determinant. Consequently, the present data show that the enzyme is multifunctional, and could be renamed ST3Gal(NAc) II. In contrast to ST3Gal II, ST3Gal III did not transfer to the X(2) pentasaccharide. The Neu5Acα2-3GalNAc linkage of sialyl X(2) was cleaved by sialidases from Arthrobacter ureafaciens and Clostridium perfringens, but resisted the action of sialidases from Newcastle disease virus and Streptococcus pneumoniae. Therefore, the latter two enzymes cannot be used to differentiate between Neu5Acα2-3GalNAc and Neu5Acα2-6GalNAc linkages, as has been assumed previously.

L10 ANSWER 4 OF 9 MEDLINE on STN DUPLICATE 2
1999292603. PubMed ID: 10362835. Characterization of the substrate specificity of alpha1,3galactosyltransferase utilizing modified N-acetyllactosamine disaccharides. Stults C L; Macher B A; Bhatti R; Srivastava O P; Hindsgaul O. (Department of Chemistry and Biochemistry, San Francisco State University 1600 Holloway Avenue, San Francisco, CA 94132, USA.) Glycobiology, **(1999 Jul)** Vol. 9, No. 7, pp. 661-8.
Journal code: 9104124. ISSN: 0959-6658. Pub. country: ENGLAND: United Kingdom. Language: English.

AB alpha1,3galactosyltransferase (alpha1,3GalT) catalyzes the synthesis of a range of **glycoconjugates** containing the Galalpha1,3Gal epitope which is recognized by the naturally occurring human antibody, anti-Gal. This enzyme may be a useful synthetic tool to produce a range of compounds to further investigate the binding site of anti-Gal and other proteins with a Galalpha1,3Gal binding site. Thus, the enzyme has been probed with a series of type 2 disaccharide-C8(Galbeta1-4GlcNAc-C8) analogs. The

enzyme tolerated acceptors with modifications at **C2** and C3 of the N-acetylglucosamine residue, producing a family of compounds with a nonreducing alpha1,3 linked **galactose**. Compounds that did not serve as acceptors were evaluated as inhibitors. Interestingly, the type 1 disaccharide-C8, Galbeta1-3GlcNAc-C8, was a good inhibitor of the enzyme (Ki = 270 microM vs. Km = 190 microM for Galbeta1-4GlcNAc-C8). A potential photoprobe, based on a modified type 2 disaccharide (octyl 3-amino-3-deoxy-3-N-(2-diazo-3, 3, 3-trifluoropropionyl-beta-D-galactopyranosyl-(1, 4)-2-acetamindo-2-deoxy-beta-D-glycopyranoside, (DTFP-LacNAc-C8)), was evaluated as an inhibitor of alpha1,3GalT. alpha1,3GalT bound DTFP-LacNAc-C8 with an affinity (Ki = 300 microM) similar to that displayed by the enzyme for LacNAc-C8. Additional studies were done to determine the enzyme's ability to transfer a range of sugars from UDP-sugar donors. The results of these experiments demonstrated that alpha1,3GalT has a strict specificity for UDP-Gal. Finally, inactivation studies with various amino acid modifiers were done to obtain information on the importance of different types of amino acids for alpha1,3GalT activity.

L10 ANSWER 5 OF 9 MEDLINE on STN DUPLICATE 3

1997292530. PubMed ID: 9147041. **Galactose**-induced dimerization of blocked ricin at acidic pH: evidence for a third **galactose** -binding site in ricin B-chain. Venkatesh Y P; Lambert J M. (ImmunoGen, Inc., Cambridge, MA 02139, USA.) Glycobiology, **(1997 Apr)** Vol. 7, No. 3, pp. 329-35. Journal code: 9104124. ISSN: 0959-6658. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Blocked ricin is a **glycoconjugate** formed by covalent modification of each of the two **galactose**-binding sites of ricin with affinity ligands derived by modification of glycopeptides containing **galactose**-terminated, triantennary, N-linked oligosaccharides. Blocked ricin undergoes a pH-dependent reversible self-association, being predominantly dimeric at neutral pH and monomeric at acidic pH. The shift in the monomer-dimer equilibrium towards the monomeric form at acidic pH (pH 4) is inhibited by lactose, as shown by size-exclusion chromatography. This behavior of blocked ricin can be reproduced in studies with isolated blocked B-chain. The effect, which is dependent on the concentration of the sugar, is specific for sugars having terminal **galactose** moieties, or sugars having the same orientation of hydroxyl groups at **C2** and C4 as **galactose**. These results are interpreted as providing further support for the notion that ricin B-chain has a third **galactose**-binding site, which may be important for the intracellular trafficking of ricin during intoxication of cells.

L10 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2009 ACS on STN

1997:216339 Document No. 126:305720 Original Reference No. 126:59223a,59226a Selectin receptors: preparation of spacer-armed sulfated trisaccharides Lewis A and Lewis X and neoglycoconjugates thereof. Zemlyanukhina, T. V.; Nifant'ev, N. E.; Shashkov, A. S.; Tsvetkov, Y. E.; Bovin, N. V. (M.M. Shemyakin Inst. Bioorganic Chem., Russian Acad. Sci., Moscow, Russia). Carbohydrate Letters, 1(4), 277-284 (English) **1995**. CODEN: CLETEC. ISSN: 1073-5070. Publisher: Harwood.

AB HSO3-3Galβ1-3(Fucα1-4)GlcNAcβ1-O(CH2)3NH2 and HSO3-3Galβ1-4-(Fucα1-3)GlcNAcβ1-O(CH2)3NH2 were synthesized by regioselective sulfation (Py·SO3Py) of protected trisaccharidic Lea and Lex derivs. bearing unsubstituted hydroxyls at **C2**, C3 and C4 of **galactose** moiety, Bn-6Galβ1-3/4(Bn3Fucα1-4/3)-6-BnGlcNAcβ1-o(CH2)3NHCOCF3, followed by conventional deprotection. Coupling of the aminopropyl glycosides with poly(4-nitrophenylacrylate) gave the resp. polyacrylamide (PAA) based conjugates. Biotinylated and fluorescent probes Sug-PAA-Biot and Sug-PAA-Flu were obtained as well.

L10 ANSWER 7 OF 9 MEDLINE on STN DUPLICATE 4

1996061943. PubMed ID: 7588738. Binding studies on the combining site of a GalNAc alpha 1-->-specific lectin with Thomsen-Friedenreich activity prepared from green marine algae Codium fragile subspecies tomentosoides. Wu A M; Song S C; Hwang P Y; Wu J H; Chang K S. (Glyco-Immunochemistry Research Lab., Institute of Molecular and Cellular Biology, Chang-Gung Medical College Tao-yuan, Taiwan.) European journal of biochemistry / FEBS, **(1995 Oct 1)** Vol. 233, No. 1, pp. 145-51. Journal code: 0107600. ISSN: 0014-2956. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB The combining site of a GalNAc alpha 1-->-specific lectin (CFT) with Thomsen-Friedenreich (T, Gal beta 1-->3-GalNAc alpha 1-->Ser/Thr) activity, purified from the subspecies tomentosoides of green marine algae Codium fragile was studied by quantitative precipitin and precipitin-inhibition assays. Of 27 glycoforms tested, Tn (GalNAc alpha 1-->Ser/Thr) glycoprotein from armadillo submandibular glands, and asialo porcine submandibular glycoprotein, which contains T, Tn and GalNAc alpha 1-->3Gal(A) sequences, completely precipitated the lectin added, and less than 1 microgram glycoprotein was required to precipitate 50% 4.7 micrograms lectin nitrogen. However, CFT precipitated negligibly with Pneumococcus type-XIV polysaccharide and asialo human alpha 1-acid glycoprotein, that contain exclusively the human blood-type-II precursor sequence (II, Gal beta 1-->4GlcNAc) at the nonreducing ends. Among the sugar inhibitors tested, the human blood A-active trisaccharide [Ah, GalNAc alpha 1-->3 (LFuc alpha 1-->2)Gal] was the best inhibitor; it was about twice as active as the T disaccharide. Oligosaccharides without GalNAc alpha 1--> as part of their sequences were inactive, indicating that the acetamido group at **C2** of **galactose** is essential for binding and that GalNAc is the main contributor in the T sequence for binding. From the data provided, it is clear that the combining site of CFT requires an alpha-anomer of GalNAc and recognizes Ah, internal GalNAc alpha 1--> of T and Tn determinants of glycans, but not the blood group I/II (Gal beta 1-->3/4GlcNAc) sequences. Consequently, CFT is a useful reagent for detecting GalNAc alpha 1-->-containing **glycoconjugates.**

L10 ANSWER 8 OF 9 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

1992:310051 Document No.: PREV199294023201; BA94:23201.

GLYCOCONJUGATES ARE STAGE AND POSITION-SPECIFIC CELL SURFACE MOLECULES IN THE DEVELOPING OLFACTORY SYSTEM 2. UNIQUE CARBOHYDRATE ANTIGENS ARE TOPOGRAPHIC MARKERS FOR SELECTIVE PROJECTION PATTERNS OF OLFACTORY AXONS. SCHWARTING G A [Reprint author]; DEUTSCH G; GATTEY D M; CRANDALL J E. DEP BIOCHEM, DEV NEUROL, E K SHRIVER CENT, WALTHAM, MASS 02254, USA. Journal of Neurobiology, (**1992**) Vol. 23, No. 2, pp. 130-142.

CODEN: JNEUBZ. ISSN: 0022-3034. Language: ENGLISH.

AB Three monoclonal antibodies specific for different carbohydrate antigens were used to analyze the development of the olfactory system in rats. CC2 antibodies react with a subset of main olfactory neurons, their axons, and terminals in the olfactory bulb. CC2 antigens are expressed on dorsomedial neurons in the olfactory epithelium (OE) from embryonic (E) day 15 to adults. In the olfactory bulb (OB), only dorsomedially located glomeruli express CC2 **glycoconjugates** from postnatal day (P) 2 to adults. Thus **C2** defines a dorsomedially organized projection that is established early in embryonic development and continues in adults. P-Path antibodies react with antigens that are expressed on the olfactory nerve in embryos, and are also detected on cell bodies in the neuroepithelium and in glomeruli of the OB at P2. At P14, P-Path staining is weaker, but remains present on many cells in the epithelium and in many glomeruli in the bulb. Postnatally, P-Path immunostaining continues to decrease in most regions of the OE and OB. At P35 and afterwards, only a

few P-Path-positive neuronal cells can be detected in the OE. Furthermore, after P35 only two groups of glomeruli in the OB are P-Path immunoreactive. One is situated adjacent to the accessory olfactory bulb (AOB) at the dorsocaudal surface of the OB. The other is adjacent to the AOB at the ventrocaudal surface of the OB. Thus, in adults, P-Path **glycoconjugates** are expressed in neurons and axons that project only to a specific subset of caudal glomeruli of the OB. Monoclonal antibody 1B2, reacts with β- **galactose**-terminating glycolipids and glycoproteins. At P2, 1B2 immunoreactivity is seen on a subset of cell bodies that are distributed throughout the OE and is expressed in most glomeruli in the OB at this age. By P35 and in adults, 1B2 continues to be expressed on a subset of neurons in the OE that project to only a small subset of glomeruli in the OB. Unlike CC2 and P-Paths antigens that define specific groups of glomeruli, 1B2-immunoreactive glomeruli do not have a detectable spatial pattern. It is more likely that 1B2 antigens define a specific stage in the maturation of connections between the OE and OB.

L10 ANSWER 9 OF 9 MEDLINE on STN DUPLICATE 5
1985081308. PubMed ID: 3965569. Complement-mediated hemolytic activity of succinylated concanavalin A: preparation and activity of cell intermediates. Langone J J; Ejzemberg R. Journal of immunology (Baltimore, Md. : 1950), **(1985 Feb)** Vol. 134, No. 2, pp. 1110-4. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB Succinylated concanavalin A (SCon A) lyses sheep erythrocytes (E) in the presence of complement, whereas the native tetravalent lectin, Con A, is inactive. We have studied the ability of E-SCon A (ES) to interact with early acting guinea pig (gp) or human (hu) complement components (C1, **C2**, C4) and found that cell intermediates ESC1, ESC4, ESC14, and ESC142 can be generated that are analogous to intermediates conventionally prepared with E and rabbit IgM (pentameric) anti-Forssman antibody. Titration of gp or hu C1, C4, and **C2**, and quantification of the number of activated C1 molecules bound to ESC4 by the C1 fixation and transfer test showed in each case that an average of one effective site per cell was sufficient to cause cell lysis. Determination of tmax for optimal formation of ESC142 sites depended on the species combination of components used to make the intermediates, and the decay of ESC142 and EAC142 sites or sites generated with ESC4, EAC4, and trypsin-activated **C2** were similar. The sugar alpha-D-methylglucopyranoside (alpha-MGP) inhibited binding of SCon A to E and eluted the lectin from ES, whereas **galactose** was nearly inactive, consistent with lectin sugar-binding selectivity. In contrast, both sugars were ineffective in eluting SCon A or C4hu from ESC4hu, indicating that C4hu blocked the interaction between lectin and alpha-MGP, perhaps by steric hindrance. SCon A is a divalent functional analogue of IgM anti-Forssman antibody that may be a uniquely suited reagent specific for cell membrane **glycoconjugates** for studying the mechanism of binding and activation of complement components.

=> s l2 and UDP-GalNAc
L11 8 L2 AND UDP-GALNAC

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PROCESSING COMPLETED FOR L11
L12 2 DUP REMOVE L11 (6 DUPLICATES REMOVED)

=> d l12 1-2 cbib abs

L12 ANSWER 1 OF 2 MEDLINE on STN DUPLICATE 1
2007347589. PubMed ID: 17370997. Direct identification of nonreducing

GlcNAc residues on N-glycans of glycoproteins using a novel **chemoenzymatic** method. Boeggeman Elizabeth; Ramakrishnan Boopathy; Kilgore Charlton; Khidekel Nelly; Hsieh-Wilson Linda C; Simpson John T; Qasba Pradman K. (Structural Glycobiology Section, CCR-Nanobiology Program, Center for Cancer Research, NCI-Frederick, Frederick, Maryland 21702, USA.) Bioconjugate chemistry, (2007 May-Jun) Vol. 18, No. 3, pp. 806-14. Electronic Publication: 2007-03-20. Journal code: 9010319. ISSN: 1043-1802. Pub. country: United States. Language: English.

AB The mutant beta1,4-galactosyltransferase (beta4Gal-T1), beta4Gal-T1-Y289L, in contrast to wild-type beta4Gal-T1, can transfer GalNAc from the sugar donor **UDP-GalNAc** to the acceptor, GlcNAc, with efficiency as good as that of galactose from UDP-Gal. Furthermore, the mutant can also transfer a modified sugar, C2 keto galactose, from its UDP derivative to O-GlcNAc modification on proteins that provided a functional handle for developing a highly sensitive **chemoenzymatic** method for detecting O-GlcNAc post-translational modification on proteins. We report herein that the modified sugar, C2 keto galactose, can be transferred to free GlcNAc residues on N-linked glycoproteins, such as ovalbumin or asialo-agalacto IgG1. The transfer is strictly dependent on the presence of both the mutant enzyme and the ketone derivative of the galactose. Moreover, the PNGase F treatment of the glycoproteins, which cleaves the N-linked oligosaccharide chain, shows that the modified sugar has been transferred to the N-glycan chains of the glycoproteins and not to the protein portion. The application of the mutant galactosyltransferase, beta4Gal-T1-Y289L, to produce **glycoconjugates** carrying sugar moieties with reactive groups, is demonstrated. We envision a broad potential for this technology such as the possibilities to link cargo molecules to glycoproteins, such as monoclonal antibodies, via glycan chains, thereby assisting in the glycotargeting of drugs to the site of action or used as biological probes.

L12 ANSWER 2 OF 2 MEDLINE on STN DUPLICATE 2

2002210359. PubMed ID: 11948877. **Chemoenzymatic** synthesis of biotinylated nucleotide sugars as substrates for glycosyltransferases. Bulter T; Schumacher T; Namdjou D J; Gutierrez Gallego R; Clausen H; Elling L. (Institute of Enzyme Technology, Heinrich-Heine University of Dusseldorf, Research Center Julich, 52426 Julich, Germany.) Chembiochem : a European journal of chemical biology, (2001 Dec 3) Vol. 2, No. 12, pp. 884-94. Journal code: 100937360. ISSN: 1439-4227. Pub. country: Germany: Germany, Federal Republic of. Language: English.

AB The enzymatic oxidation of uridine 5'-diphospho-alpha-D-galactose (UDP-Gal) and uridine 5'-diphospho-N-acetyl-alpha-D-galactosamine (**UDP-GalNAc**) with galactose oxidase was combined with a chemical biotinylation step involving biotin-epsilon-amidocaproylhydrazide in a one-pot synthesis. The novel nucleotide sugar derivatives uridine 5'-diphospho-6-biotin-epsilon-amidocaproylhydrazino-alpha-D-galactose (UDP-6-biotinyl-Gal) and uridine 5'-diphospho-6-biotin-epsilon-amidocaproylhydrazino-N-acetyl-alpha-D-galactosamine (UDP-6-biotinyl-GalNAc) were synthesized on a 100-mg scale and characterized by mass spectrometry (fast atom bombardment and matrix-assisted laser desorption/ionization time of flight) and one/two dimensional NMR spectroscopy. It could be demonstrated for the first time, by use of UDP-6-biotinyl-Gal as a donor substrate, that the human recombinant galactosyltransferases beta3Gal-T5, beta4Gal-T1, and beta4Gal-T4 mediate biotinylation of the neoglycoconjugate bovine serum albumin-p-aminophenyl N-acetyl-beta-D-glucosaminide (BSA-(GlcNAc)17) and ovalbumin. The detection of the biotin tag transferred by beta3Gal-T5 onto BSA-(GlcNAc)17 with streptavidin-enzyme conjugates gave detection limits of 150 pmol of tagged GlcNAc in a Western blot analysis and 1 pmol of tagged GlcNAc in a microtiter plate assay. The degree of Gal-biotin tag transfer onto agalactosylated hybrid N-glycans present at the single

glycosylation site of ovalbumin was dependent on the Gal-T used (either beta3Gal-T5, beta4Gal-T4, or beta4Gal-T1), which indicates that the acceptor specificity may direct the transfer of the Gal-biotin tag. The potential of this biotinylated UDP-Gal as a novel donor substrate for human galactosyltransferases lies in the targeting of distinct acceptor structures, for example, under-galactosylated **glycoconjugates**, which are related to diseases, or in the quality control of glycosylation of recombinant and native glycoproteins.

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=> s l1 and C2
L13        125 L1 AND C2

=> s l13 and keto
L14         11 L13 AND KETO

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L15         10 L14 AND GALACTOSE

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L16           2 DUP REMOVE L15 (8 DUPLICATES REMOVED)

=> d l16 1-2 cbib abs

L16  ANSWER 1 OF 2     MEDLINE on STN                    DUPLICATE 1
2009214372.    PubMed ID: 19245254.   Bioconjugation and Detection of
     Lactosamine Moiety using alpha1,3-Galactosyltransferase Mutants That
     Transfer C2-Modified Galactose with a Chemical Handle.
     Pasek Marta; Ramakrishnan Boopathy; Boeggeman Elizabeth; Manzoni Maria;
     Waybright Timothy J; Qasba Pradman K. (Structural Glycobiology Section,
     Nanobiology Program, NCI-Frederick, Basic Research Program, and Laboratory
     of Proteomics and Analytical Technologies, SAIC-Frederick, Inc., Center
     for Cancer Research, NCI-Frederick, Frederick, Maryland 21702. )
     Bioconjugate chemistry, (2009 Mar) Vol. 20, No. 3, pp. 608-18.  Journal
     code: 9010319. E-ISSN: 1520-4812. Pub. country: United States. Language:
     English.
AB   Studies on wild-type and mutant glycosyltransferases have shown that they
     can transfer modified sugars with a versatile chemical handle, such as
     keto or azido group, that can be used for conjugation chemistry
     and detection of glycan residues on glycoconjugates.  To detect
     the most prevalent glycan epitope, N-acetyllactosamine (LacNAc
     (Galbeta1-4GalNAcbeta)), we have mutated a bovine
     alpha1,3-galactosyltransferse (alpha3Gal-T)() enzyme which normally
     transfers Gal from UDP-Gal to the LacNAc acceptor, to transfer GalNAc or
     C2-modified galactose from their UDP derivatives.  The
     alpha3Gal-T enzyme belongs to the alpha3Gal/GalNAc-T family that includes
     human blood group A and B glycosyltransferases, which transfer GalNAc and
     Gal, respectively, to the Gal moiety of the trisaccharide
     Fucalpha1-2Galbeta1-4GlcNAc.  On the basis of the sequence and structure
     comparison of these enzymes, we have carried out rational mutation studies
     on the sugar donor-binding residues in bovine alpha3Gal-T at positions 280
     to 282.  A mutation of His280 to Leu/Thr/Ser/Ala or Gly and Ala281 and
     Ala282 to Gly resulted in the GalNAc transferase activity by the mutant
     alpha3Gal-T enzymes to 5-19% of their original Gal-T activity.  We show
     that the mutants (280)SGG(282) and (280)AGG(282) with the highest GalNAc-T
     activity can also transfer modified sugars such as 2-keto-
     galactose or GalNAz from their respective UDP-sugar derivatives to
     LacNAc moiety present at the nonreducing end of glycans of asialofetuin,
     thus enabling the detection of LacNAc moiety of glycoproteins and
     glycolipids by a chemiluminescence method.
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L16 ANSWER 2 OF 2 MEDLINE on STN DUPLICATE 2
2007347589. PubMed ID: 17370997. Direct identification of nonreducing GlcNAc residues on N-glycans of glycoproteins using a novel chemoenzymatic method. Boeggeman Elizabeth; Ramakrishnan Boopathy; Kilgore Charlton; Khidekel Nelly; Hsieh-Wilson Linda C; Simpson John T; Qasba Pradman K. (Structural Glycobiology Section, CCR-Nanobiology Program, Center for Cancer Research, NCI-Frederick, Frederick, Maryland 21702, USA.) Bioconjugate chemistry, (2007 May-Jun) Vol. 18, No. 3, pp. 806-14. Electronic Publication: 2007-03-20. Journal code: 9010319. ISSN: 1043-1802. Pub. country: United States. Language: English.

AB The mutant beta1,4-galactosyltransferase (beta4Gal-T1), beta4Gal-T1-Y289L, in contrast to wild-type beta4Gal-T1, can transfer GalNAc from the sugar donor UDP-GalNAc to the acceptor, GlcNAc, with efficiency as good as that of **galactose** from UDP-Gal. Furthermore, the mutant can also transfer a modified sugar, **C2 keto galactose**, from its UDP derivative to O-GlcNAc modification on proteins that provided a functional handle for developing a highly sensitive chemoenzymatic method for detecting O-GlcNAc post-translational modification on proteins. We report herein that the modified sugar, **C2 keto galactose**, can be transferred to free GlcNAc residues on N-linked glycoproteins, such as ovalbumin or asialo-agalacto IgG1. The transfer is strictly dependent on the presence of both the mutant enzyme and the ketone derivative of the **galactose**. Moreover, the PNGase F treatment of the glycoproteins, which cleaves the N-linked oligosaccharide chain, shows that the modified sugar has been transferred to the N-glycan chains of the glycoproteins and not to the protein portion. The application of the mutant galactosyltransferase, beta4Gal-T1-Y289L, to produce **glycoconjugates** carrying sugar moieties with reactive groups, is demonstrated. We envision a broad potential for this technology such as the possibilities to link cargo molecules to glycoproteins, such as monoclonal antibodies, via glycan chains, thereby assisting in the glycotargeting of drugs to the site of action or used as biological probes.

=> s l1 and EC2.1.1.38
L17 0 L1 AND EC2.1.1.38

=> s l1 and GlcNAc
L18 1528 L1 AND GLCNAC

=> s l18 and C2
L19 22 L18 AND C2

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PROCESSING COMPLETED FOR L19
L20 9 DUP REMOVE L19 (13 DUPLICATES REMOVED)

=> d l20 1-9 cbib abs

L20 ANSWER 1 OF 9 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN
2009:520110 The Genuine Article (R) Number: 436QJ. Identification and characterization of flavonoids as sialyltransferase inhibitors. Hidari, Kazuya I. P. J. (Reprint). Univ Shizuoka, Dept Biochem, Sch Pharmaceut Sci, Japan & Global COE Program, Suruga Ku, 52-1 Yada, Shizuoka 4228526, Japan (Reprint). E-mail: hidari@u-shizuoka-ken.ac.jp. Hidari, Kazuya I. P. J. (Reprint); Goto, Shiho; Kanai, Yugo; Watanabe, Kei-ichi; Suzuki, Takashi. Univ Shizuoka, Dept Biochem, Sch Pharmaceut Sci, Japan & Global COE Program, Suruga Ku, Shizuoka 4228526, Japan. E-mail: hidari@u-shizuoka-ken.ac.jp. Oyama, Kin-ichi. Nagoya Univ, Res Ctr Mat

Sci, Chem Instrument Facil, Nagoya, Aichi 4648601, Japan. Ito, Go; Nakayama, Miho; Inai, Makoto; Furuta, Takumi; Kan, Toshiyuki. Univ Shizuoka, Dept Synth Organ & Med Chem, Sch Pharmaceut Sci, Japan & Global COE Program, Suruga Ku, Shizuoka 4228526, Japan. Yoshida, Kumi. Nagoya Univ, Grad Sch Informat Sci, Nagoya, Aichi 4648601, Japan.
BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS (8 MAY 2009) Vol. 382, No. 3, pp. 609-613. ISSN: 0006-291X. Publisher: ACADEMIC PRESS INC ELSEVIER SCIENCE, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495 USA.
Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Sialyltransferases biosynthesize sialyl-**glycoconjugates** involved in many biological and pathological processes. We investigated and characterized synthetic flavonoid derivatives as sialyltransferase inhibitors. We first examined 54 compounds by solid-phase enzyme assay using beta-galactoside alpha 2,6-sialyltransferase 1 (ST6Gal I) and beta-galactoside alpha 2,3-sialyltransferase. Several compounds inhibited sialyltransferase enzyme activity regardless of sialyl-linkage reactions. Among them, two compounds showed inhibitory activity against ST6Gal I with IC50 values less than 10 mu M. Three characteristic features of flavonoids were determined by structure-inhibitory activity relationships. First, a double bond between **C2**-C3 linkages is required for the activity. Second, increasing hydrophilic properties on the B-ring markedly augmented the inhibitory effect. Third, a hydrophobic functional group introduced on the hydroxyl groups of the A-ring enhanced the inhibitory activity. Kinetic analysis using human ST6Gal I indicated a mixed inhibition mechanism of the compounds. In conclusion, the flavonoids identified could be applied for control of cellular expression of sialic acid.

L20 ANSWER 2 OF 9 MEDLINE on STN DUPLICATE 1

2008368926. PubMed ID: 18426242. Site-specific linking of biomolecules via glycan residues using glycosyltransferases. Qasba Pradman K; Boeggeman Elizabeth; Ramakrishnan Boopathy. (Structural Glycobiology Section, SAIC-Frederick, Inc., Center for Cancer Research Nanobiology Program, Center for Cancer Research, NCI-Frederick, Frederick, Maryland 21702, USA.. qasba@helix.nih.gov) . Biotechnology progress, (2008 May-Jun) Vol. 24, No. 3, pp. 520-6. Electronic Publication: 2008-04-22. Ref: 42.
Journal code: 8506292. E-ISSN: 1520-6033.
Report No.: NLM-NIHMS46121; NLM-PMC2435414. Pub. country: United States.
Language: English.

AB The structural information on glycosyltransferases has revealed that the sugar-donor specificity of these enzymes can be broadened to include modified sugars with a chemical handle that can be utilized for conjugation chemistry. Substitution of Tyr289 to Leu in the catalytic pocket of bovine beta-1,4-galactosyltransferase generates a novel glycosyltransferase that can transfer not only Gal but also GalNAc or a **C2**-modified galactose that has a chemical handle, from the corresponding UDP-derivatives, to the non-reducing end **GlcNAc** residue of a **glycoconjugate**. Similarly, the wild-type polypeptide-N-acetyl-galactosaminyltransferase, which naturally transfers GalNAc from UDP-GalNAc, can also transfer **C2**-modified galactose with a chemical handle from its UDP-derivative to the Ser/Thr residue of a polypeptide acceptor substrate that is tagged as a fusion peptide to a non-glycoprotein. The potential of wild-type and mutant glycosyltransferases to produce **glycoconjugates** carrying sugar moieties with chemical handle makes it possible to conjugate biomolecules with orthogonal reacting groups at specific sites. This methodology assists in the assembly of bio-nanoparticles that are useful for developing targeted drug-delivery systems and contrast agents for magnetic resonance imaging.

L20 ANSWER 3 OF 9 MEDLINE on STN DUPLICATE 2

2007347589. PubMed ID: 17370997. Direct identification of nonreducing **GlcNAc** residues on N-glycans of glycoproteins using a novel chemoenzymatic method. Boeggeman Elizabeth; Ramakrishnan Boopathy; Kilgore Charlton; Khidekel Nelly; Hsieh-Wilson Linda C; Simpson John T; Qasba Pradman K. (Structural Glycobiology Section, CCR-Nanobiology Program, Center for Cancer Research, NCI-Frederick, Frederick, Maryland 21702, USA.) Bioconjugate chemistry, (2007 May-Jun) Vol. 18, No. 3, pp. 806-14. Electronic Publication: 2007-03-20. Journal code: 9010319. ISSN: 1043-1802. Pub. country: United States. Language: English.

AB The mutant beta1,4-galactosyltransferase (beta4Gal-T1), beta4Gal-T1-Y289L, in contrast to wild-type beta4Gal-T1, can transfer GalNAc from the sugar donor UDP-GalNAc to the acceptor, **GlcNAc**, with efficiency as good as that of galactose from UDP-Gal. Furthermore, the mutant can also transfer a modified sugar, **C2** keto galactose, from its UDP derivative to O-**GlcNAc** modification on proteins that provided a functional handle for developing a highly sensitive chemoenzymatic method for detecting O-**GlcNAc** post-translational modification on proteins. We report herein that the modified sugar, **C2** keto galactose, can be transferred to free **GlcNAc** residues on N-linked glycoproteins, such as ovalbumin or asialo-agalacto IgG1. The transfer is strictly dependent on the presence of both the mutant enzyme and the ketone derivative of the galactose. Moreover, the PNGase F treatment of the glycoproteins, which cleaves the N-linked oligosaccharide chain, shows that the modified sugar has been transferred to the N-glycan chains of the glycoproteins and not to the protein portion. The application of the mutant galactosyltransferase, beta4Gal-T1-Y289L, to produce **glycoconjugates** carrying sugar moieties with reactive groups, is demonstrated. We envision a broad potential for this technology such as the possibilities to link cargo molecules to glycoproteins, such as monoclonal antibodies, via glycan chains, thereby assisting in the glycotargeting of drugs to the site of action or used as biological probes.

L20 ANSWER 4 OF 9 MEDLINE on STN DUPLICATE 3

2004289406. PubMed ID: 15189346. Transfection of 2,6 and 2,3-sialyltransferase genes and **GlcNAc**-transferase genes into human glioma cell line U-373 MG affects **glycoconjugate** expression and enhances cell death. Dawson G; Moskal J R; Dawson S A. (Department of Pediatrics MC 4068, University of Chicago School of Medicine, 5841 S. Maryland Avenue, Chicago, IL 60637, USA.. dawg@midway.uchicago.edu) . Journal of neurochemistry, (2004 Jun) Vol. 89, No. 6, pp. 1436-44. Journal code: 2985190R. ISSN: 0022-3042. Pub. country: England: United Kingdom. Language: English.

AB Human glioma cell line U-373 MG expresses CMP-NeuAc : Galbeta1,3GlcNAc alpha2,3-sialyltransferase [EC Number 2.4.99.6] (alpha2,3ST), UDP-**GlcNAc** : beta-d-mannoside beta1,6-N-acetylglucosaminyltransferase V [EC 2.4.1.155] (GnT-V) and UDP-GlcNAc3: beta-d-mannoside beta1,4-N-acetylglucosaminyltransferase III [EC 2.4.1.144] (GnT-III) but not CMP-NeuAc : Galbeta1,4GlcNAc alpha2,6-sialyltransferase [EC 2.4.99.1] (alpha2,6ST) under normal culture conditions. We have previously shown that transfection of the alpha2,6ST gene into U-373 cells replaced alpha2,3-linked sialic acids with alpha2,6 sialic acids, resulting in a marked inhibition of glioma cell invasivity and a significant reduction in adhesivity. We now show that U-373 cells, which are typically highly resistant to cell death induced by chemotherapeutic agents (< 10% death in 18 h), become more sensitive to apoptosis following overexpression of these four glycoprotein glycosyltransferases. U-373 cell viability showed a three-fold decrease (from 20 to 60% cell death) following treatment with staurosporine, **C2**-ceramide or etoposide, when either alpha2,6ST and GnT-V genes were stably overexpressed. Even glycosyltransferases typically raised in cancer cells, such as alpha2,3ST and GnT-III, were able to decrease viability two-fold (from 20 to 40% cell death) following

stable overexpression. The increased susceptibility of glycosyltransferase-transfected U-373 cells to pro-apoptotic drugs was associated with increased ceramide levels in Rafts, increased caspase-3 activity and increased DNA fragmentation. In contrast, the same glycosyltransferase overexpression protected U-373 cells against a different class of apoptotic drugs, namely the phosphatidylinositol 3-kinase inhibitor LY294002. Thus altered surface protein glycosylation of a human glioblastoma cell line can lead to lowered resistance to chemotherapeutic agents.

L20 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2009 ACS on STN
2005:152076 Document No. 143:212062 Transglycosylation and condensation of disaccharide units using endo-type glycosidases. Totani, Kazuhide; Yasutake, Nozomu; Murata, Takeomi; Usui, Taichi (Department of Chemical Engineering, Ichinoseki National College of Technology, Hagisho, Ichinoseki City, Iwate, 021-8511, Japan). Trends in Glycoscience and Glycotechnology, 16(92), 383-392 (English/Japanese) 2004. CODEN: TGGLEE. ISSN: 0915-7352. Publisher: FCCA.
AB A review with refs. Two kinds of synthetic methods using transglycosylation or condensation with disaccharide units by endo-glycosidases have been developed. First, in a com. available cellulase preparation of Trichoderma reesei, we found transglycosylation activity enabling it to transfer the entire lactose (Lac) and N-acetyllactosamine (LacNAc) from p-nitrophenyl β-lactoside (Lacβ-pNP) and p-nitrophenyl β-N-acetyllactosaminide (LaCNAcβ-pNP), resp. Using the enzyme activities, various β-lactosides such as alkyl β-lactosides were directly synthesized. The enzyme catalyzed not only transglycosylation but also condensation reaction between the disaccharides and aglycons. Although 1-alkanols, 2-alkanols, alkan-diols, allyl alc., glycerol, Man and Glc can be acceptors for transfer of the disaccharide units, the efficiency of transglycosylation and condensation decreased with the increase in length of the alkyl chain of alkanol acceptors from **C2** to C12. The yield of condensation between lactose and glycerol reached up to 40% by elimination of coexistent β-galactosidases. Condensation using the enzyme enabled practical synthesis of various glycosides possessing Lac and LacNAc units and offered a novel method for enzymic synthesis of neoglycolipid precursors. The results of purification of crude enzyme preparation followed by a substrate competition assay on LacNAcβ-pNP hydrolysis indicated that both transglycosylation and condensation are mediated by a single enzyme, which is thought to be one of the endo-β-(1-4)-glucanases. Next, endo-β-galactosidase from Escherichia freundii, which has been used for structural and functional analyses of glycans involved in **glycoconjugates**, was shown to catalyze regioselective transfer of the **GlcNAc**.beta.1-3Gal unit onto the OH-4 position of non-reducing end **GlcNAc** of acceptor substrates. As a result, the transglycosylation led to facile preparation of LacNAc-repeating oligosaccharides.

L20 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2009 ACS on STN
2001:52655 Document No. 134:2484030 Ketone Isosteres of 2-N-Acetamidosugars as Substrates for Metabolic Cell Surface Engineering. Hang, Howard C.; Bertozzi, Carolyn R. (Departments of Chemistry, University of California, Berkeley, CA, 94720, USA). Journal of the American Chemical Society, 123(6), 1242-1243 (English) 2001. CODEN: JACSAT. ISSN: 0002-7863. OTHER SOURCES: CASREACT 134:248403. Publisher: American Chemical Society.
AB Metabolic oligosaccharide engineering using unnatural substrates has provided an avenue for the introduction of novel chemical reactivity on cell surfaces. This approach exploits the unnatural substrate tolerance of enzymes involved in carbohydrate biosynthesis. For example, derivs. of N-acetylmannosamine (ManNAc) which bear a selectively reactive chemical

handle, such as a ketone or azide, on the N-acyl group are transformed into **glycoconjugate**-bound sialosides by human cells. The selective reactivity of ketones with aminooxy or hydrazide groups, and azides with modified phosphine reagents, permits exogenous chemical cell surface targeting. If the substrate promiscuity exhibited by the enzymes and transporters of the sialic acid pathway is a general feature of other carbohydrate metabolic pathways, multiple avenues for metabolic engineering will be available. So far, few studies have addressed the unnatural substrate tolerance of other carbohydrate biosynthetic pathways. The ubiquitous presence of the 2-N-acetamidosugars, N-acetylglucosamine (**GlcNAc**) and N-acetylgalactosamine (GalNAc), in glycoproteins, proteoglycans, and glycolipids makes them attractive targets for metabolic engineering. **GlcNAc** and GalNAc are converted within cells to their UDP-activated analogs via salvage pathways. UDP-**GlcNAc** can be subsequently converted to ManNAc or UDP-GalNAc, or utilized by **GlcNAc** transferases that incorporate the sugar into various **glycoconjugates**. Likewise, GalNAc transferases utilize UDP-GalNAc as a substrate and deliver the sugar to numerous **glycoconjugates** . We considered the possibility that unnatural **GlcNAc** and GalNAc derivs. might gain access to the cell surface through their resp. salvage pathways. We designed 2-ketosugars, which are **C2**-carbon isosteres of the 2-N-acetamidosugars, as novel analogs that possess a ketone group for chemoselective reaction with aminooxy or hydrazide reagents. A concise synthesis of 2-ketosugars was developed from known 2-iodosugars, which are readily available by electrophilic iodination of com. available glycals. The cellular metabolism of the 2-ketosugars was investigated in a number of cell lines which exhibit varying patterns of N- and O-linked glycosylation. In conclusion, we have demonstrated that a 2-keto isostere of GalNAc is a novel substrate for metabolic glycoprotein engineering in wild-type and ldl-D CHO cells. The corresponding **GlcNAc** analog could not be detected on cells of any type, perhaps due to competition with endogenous **GlcNAc** and its downstream intermediates in the salvage pathway which are present at notoriously high intracellular concns. The 2-keto GalNAc analog should be incorporated into secreted glycoproteins as well as cell surface mols., since both are similarly post-translationally modified. This technique might be exploited to introduce unique chemical reactivity into secreted glycoproteins produced by large-scale recombinant expression, allowing further selective modification.

L20 ANSWER 7 OF 9 MEDLINE on STN DUPLICATE 4

2000112787. PubMed ID: 10644682. Binding of Clostridium botulinum **C2** toxin to asparagine-linked complex and hybrid carbohydrates. Eckhardt M; Barth H; Blocker D; Aktories K. (Institut fur Pharmakologie und Toxikologie der Albert-Ludwigs-Universitat Freiburg, Hermann-Herder-Strasse 5, D-79104 Freiburg, Germany.) The Journal of biological chemistry, (2000 Jan 28) Vol. 275, No. 4, pp. 2328-34. Journal code: 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.

AB Clostridium botulinum **C2** toxin is a binary toxin composed of an enzymatic subunit (C2I) capable of ADP-ribosylating actin and a binding subunit (C2II) that is responsible for interaction with receptors on eukaryotic cells. Here we show that binding of **C2** toxin depends on the presence of asparagine-linked carbohydrates. A recently identified Chinese hamster ovary cell mutant (Fritz, G., Schroeder, P., and Aktories, K. (1995) Infect. Immun. 63, 2334-2340) was found to be deficient in N-acetylglucosaminyltransferase I. **C2** sensitivity of this mutant was restored by transfection of an N-acetylglucosaminyltransferase I cDNA. **C2** toxin sensitivity was reduced after inhibition of alpha-mannosidase II. In contrast, Chinese hamster ovary cell mutants deficient in sialylated (Lec2) or galactosylated (Lec8) **glycoconjugates** showed an increase in toxin sensitivity compared

with wild-type cells. Our results show that the **GlcNAc** residue linked beta-1,2 to the alpha-1,3-mannose of the asparagine-linked core structure is essential for C2II binding to Chinese hamster ovary cells.

L20 ANSWER 8 OF 9 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN

1999:475394 The Genuine Article (R) Number: 208MG. Characterization of the substrate specificity of alpha 1,3galactosyltransferase utilizing modified N-acetyllactosamine disaccharides.

Macher B A (Reprint). San Francisco State Univ, Dept Chem & Biochem, 1600 Holloway Ave, San Francisco, CA 94132 USA (Reprint). Stults C L M; Bhatti R; Srivastava O P; Hindsgaul O. San Francisco State Univ, Dept Chem & Biochem, San Francisco, CA 94132 USA; Alberta Res Council, Edmonton, AB T6H 5X2, Canada; Univ Alberta, Dept Chem, Edmonton, AB T6G 2G2, Canada. GLYCOBIOLOGY (JUL 1999) Vol. 9, No. 7, pp. 661-668. ISSN: 0959-6658. Publisher: OXFORD UNIV PRESS INC, JOURNALS DEPT, 2001 EVANS RD, CARY, NC 27513 USA. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB alpha 1,3galactosyltransferase (alpha 1,3GalT) catalyzes the synthesis of a range of **glycoconjugates** containing the Gal alpha 1,3Gal epitope which is recognized by the naturally occurring human antibody, anti-Gal. This enzyme may be a useful synthetic tool to produce a range of compounds to further investigate the binding site of anti-Gal and other proteins with a Gal alpha 1,3Gal binding site. Thus, the enzyme has been probed with a series of type 2 disaccharide-C-8 (Gal beta 1-4GlcNAc-C-8) analogs. The enzyme tolerated accepters with modifications at **C2** and C3 of the N-acetylglucosamine residue, producing a family of compounds with a nonreducing alpha 1,3 linked galactose, Compounds that did not serve as accepters mere evaluated as inhibitors. Interestingly the type 1 disaccharide-C-8, Gal beta 1-3GlcNAc-C-8, was a good inhibitor of the enzyme (Ki = 270 mu M vs. Km = 190 mu M for Gal beta 1-4GlcNAc-C-8), A potential photoprobe, based on a modified type 2 disaccharide (octyl 3-amino-3-deoxy-3-N-(2-diazo-3, 3, 3-trifluoropropionyl-beta-D-galactopyranosyl-(1, 4)-2-acetamindo-2-deoxy-beta-D-glycopyranoside, (DTFP-LacNAc-C-8)), was evaluated as an inhibitor of alpha 1,3GalT. alpha 1,3GalT bound DTFP-LacNAc-C-8 with an affinity (Ki = 300 mu M) similar to that displayed by the enzyme for LacNAc-C-8, Additional studies mere done to determine the enzyme's ability to transfer a range of sugars from UDP-sugar donors. The results of these experiments demonstrated that alpha 1,3GalT has a strict specificity for UDP-Gal. Finally, inactivation studies with various amino acid modifiers mere done to obtain information on the importance of different types of amino acids for alpha 1,3GalT activity.

L20 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2009 ACS on STN

1997:216339 Document No. 126:305720 Original Reference No. 126:59223a,59226a Selectin receptors: preparation of spacer-armed sulfated trisaccharides Lewis A and Lewis X and neoglycoconjugates thereof. Zemlyanukhina, T. V.; Nifant'ev, N. E.; Shashkov, A. S.; Tsvetkov, Y. E.; Bovin, N. V. (M.M. Shemyakin Inst. Bioorganic Chem., Russian Acad. Sci., Moscow, Russia). Carbohydrate Letters, 1(4), 277-284 (English) 1995. CODEN: CLETEC. ISSN: 1073-5070. Publisher: Harwood.

AB HSO3-3Galβ1-3(Fucα1-4) **GlcNAc**.beta.1-O(CH2)3NH2 and HSO3-3Galβ1-4-(Fucα1-3) **GlcNAc**.beta.1-O(CH2)3NH2 were synthesized by regioselective sulfation (Py·SO3Py) of protected trisaccharidic Lea and Lex derivs. bearing unsubstituted hydroxyls at **C2**, C3 and C4 of galactose moiety, Bn-6Galβ1-3/4(Bn3Fucα1-4/3)-6-BnGlcNAcβ1-o(CH2)3NHCOCF3, followed by conventional deprotection. Coupling of the aminopropyl glycosides with poly(4-nitrophenylacrylate) gave the resp. polyacrylamide (PAA) based conjugates. Biotinylated and fluorescent probes Sug-PAA-Biot and Sug-PAA-Flu were obtained as well.

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---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	133.91	134.13

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
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PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

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NEWS 2	APR 02	CAS Registry Number Crossover Limits Increased to 500,000 in Key STN Databases
NEWS 3	APR 02	PATDPAFULL: Application and priority number formats enhanced
NEWS 4	APR 02	DWPI: New display format ALLSTR available
NEWS 5	APR 02	New Thesaurus Added to Derwent Databases for Smooth Sailing through U.S. Patent Codes
NEWS 6	APR 02	EMBASE Adds Unique Records from MEDLINE, Expanding Coverage back to 1948
NEWS 7	APR 07	CA/CAplus CLASS Display Streamlined with Removal of Pre-IPC 8 Data Fields
NEWS 8	APR 07	50,000 World Traditional Medicine (WTM) Patents Now Available in CAplus
NEWS 9	APR 07	MEDLINE Coverage Is Extended Back to 1947
NEWS 10	JUN 16	WPI First View (File WPIFV) will no longer be available after July 30, 2010
NEWS 11	JUN 18	DWPI: New coverage - French Granted Patents
NEWS 12	JUN 18	CAS and FIZ Karlsruhe announce plans for a new STN platform
NEWS 13	JUN 18	IPC codes have been added to the INSPEC backfile

(1969-2009)
NEWS 14 JUN 21 Removal of Pre-IPC 8 data fields streamline displays in CA/CAplus, CASREACT,and MARPAT
NEWS 15 JUN 21 Access an additional 1.8 million records exclusively enhanced with 1.9 million CAS Registry Numbers -- EMBASE Classic on STN
NEWS 16 JUN 28 Introducing "CAS Chemistry Research Report": 40 Years of Biofuel Research Reveal China Now Atop U.S. in Patenting and Commercialization of Bioethanol
NEWS 17 JUN 29 Enhanced Batch Search Options in DGENE, USGENE, and PCTGEN
NEWS 18 JUL 19 Enhancement of citation information in INPADOC databases provides new, more efficient competitor analyses
NEWS 19 JUL 26 CAS coverage of global patent authorities has expanded to 61 with the addition of Costa Rica
NEWS 20 SEP 09 New basic patent number increases precision in retrieving records from USGENE

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=> file medline hcaplus biosis embase scisearch
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 0.22 0.22

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FILE 'HCAPLUS' ENTERED AT 17:37:23 ON 10 SEP 2010
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=> s glycoconjugate
L1 35701 GLYCOCONJUGATE

```
=> and l1 and GalNAc
AND IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s l1 and "GalNAc"
L2        1621 L1 AND "GALNAC"

=> s l2 and UDP-Gal-Keto
L3           0 L2 AND UDP-GAL-KETO

=> s l1 and 2-keto-Gal
L4           1 L1 AND 2-KETO-GAL

=> d l4 cbib abs

L4   ANSWER 1 OF 1  EMBASE  COPYRIGHT (c) 2010 Elsevier B.V. All rights
     reserved on STN
2009361006  EMBASE  Multiple site-specific in vitro labeling of single-chain
     antibody.
     Ramakrishnan, Boopathy; Boeggeman, Elizabeth; Manzoni, Maria; Qasba,
     Pradman K.. Structural Glycobiology Section, Center for Cancer Research,
     NCI-Frederick, Frederick, MD 21702, United States. qasba@helix.nih.gov.
     Zhu, Zhongyu; Dimitrov, Dimiter S.. Protein Interaction Group, Center for
     Cancer Research, NCI-Frederick, Frederick, MD 21702, United States.
     Loomis, Kristin; Puri, Anu. Membrane Structure and Function Section,
     Center for Cancer Research, NCI-Frederick, Frederick, MD 21702, United
     States. Ramakrishnan, Boopathy; Boeggeman, Elizabeth; Zhu, Zhongyu. Basic
     Research Program, Center for Cancer Research, NCI-Frederick, Frederick, MD
     21702, United States. Qasba, P. K. (correspondence). Structural
     Glycobiology Section, Center for Cancer Research, NCI-Frederick,
     Frederick, MD 21702, United States. qasba@helix.nih.gov.
     Bioconjugate Chemistry  Vol. 20, No. 7, pp. 1383-1389  15 Jul 2009.
     Refs: 22.
     ISSN: 1043-1802. CODEN: BCCHES.
     American Chemical Society, 2540 Olentangy River Road, P.O. Box 3337,
     Columbus, OH 43210-3337, United States.
     Pub. Country: United States. Language: English. Summary Language: English.
     Entered STN: 20090825. Last Updated on STN: 20090825
AB   For multiple site-specific conjugations of bioactive molecules to a
     single-chain antibody (scFv) molecule, we have constructed a human anti
     HER2 receptor, scFv, with a C-terminal fusion polypeptide containing 1, 3,
     or 17 threonine (Thr) residues.  The C-terminal extended fusion
     polypeptides of these recombinant scFv fusion proteins are used as the
     acceptor substrate for human polypeptide-R-α-
     acetylgalactosaminyltransferase II (h-ppGalNAc-T2) that transfers either
     GalNAc or 2-keto-Gal, a modified galactose
     with a chemical handle, from their respective UDP-sugars to the side-chain
     hydroxyl group of the Thr residue(s).  The recombinant scFv fusion
     proteins are expressed in E. coli as inclusion bodies and in Vitro
     refolded and glycosylated with h-ppGalNAc-T2.  Upon protease cleavage, the
     MALDI-TOF spectra of the glycosylated C-terminal fusion polypeptides
     showed that the glycosylated scFv fusion protein with a single Thr residue
     is fully glycosylated with a single 2-keto-Gal
     , whereas the glycosylated scFv fusion protein with 3 and 17 Thr residues
     is found as an equal mixture of 2-3 and 5-8 2-keto-
     Gal glycosylated fusion proteins, respectively.  These fusion scFv
     proteins with the modified galactose are then conjugated with a
     fluorescence probe, Alexa488, that carries an orthogonal reactive group.
     The fluorescence labeled scFv proteins bind specifically to a human breast
```

cancer cell line (SK-BR-3) that overexpresses the HER2 receptor, indicating that the in Vitro folded scFv fusion proteins are biologically active and the presence of conjugated multiple Alexa488 probes in their C-terminal end does not interfere with their binding to the antigen. .COPYRGT. 2009 American Chemical Society.

=> s l1 and Gal-Keto
L5 0 L1 AND GAL-KETO

=> s l1 and "Y289L"
L6 5 L1 AND "Y289L"

=> dup remove l6
PROCESSING COMPLETED FOR L6
L7 1 DUP REMOVE L6 (4 DUPLICATES REMOVED)

=> d l7 cbib abs

L7 ANSWER 1 OF 1 MEDLINE on STN DUPLICATE 1
2007347589. PubMed ID: 17370997. Direct identification of nonreducing GlcNAc residues on N-glycans of glycoproteins using a novel chemoenzymatic method. Boeggeman Elizabeth; Ramakrishnan Boopathy; Kilgore Charlton; Khidekel Nelly; Hsieh-Wilson Linda C; Simpson John T; Qasba Pradman K. (Structural Glycobiology Section, CCR-Nanobiology Program, Center for Cancer Research, NCI-Frederick, Frederick, Maryland 21702, USA.) Bioconjugate chemistry, (2007 May-Jun) Vol. 18, No. 3, pp. 806-14. Electronic Publication: 2007-03-20. Journal code: 9010319. ISSN: 1043-1802. L-ISSN: 1043-1802. Pub. country: United States. Language: English.

AB The mutant beta1,4-galactosyltransferase (beta4Gal-T1), beta4Gal-T1-**Y289L**, in contrast to wild-type beta4Gal-T1, can transfer GalNAc from the sugar donor UDP-GalNAc to the acceptor, GlcNAc, with efficiency as good as that of galactose from UDP-Gal. Furthermore, the mutant can also transfer a modified sugar, C2 keto galactose, from its UDP derivative to O-GlcNAc modification on proteins that provided a functional handle for developing a highly sensitive chemoenzymatic method for detecting O-GlcNAc post-translational modification on proteins. We report herein that the modified sugar, C2 keto galactose, can be transferred to free GlcNAc residues on N-linked glycoproteins, such as ovalbumin or asialo-agalacto IgG1. The transfer is strictly dependent on the presence of both the mutant enzyme and the ketone derivative of the galactose. Moreover, the PNGase F treatment of the glycoproteins, which cleaves the N-linked oligosaccharide chain, shows that the modified sugar has been transferred to the N-glycan chains of the glycoproteins and not to the protein portion. The application of the mutant galactosyltransferase, beta4Gal-T1-**Y289L**, to produce **glycoconjugates** carrying sugar moieties with reactive groups, is demonstrated. We envision a broad potential for this technology such as the possibilities to link cargo molecules to glycoproteins, such as monoclonal antibodies, via glycan chains, thereby assisting in the glycotargeting of drugs to the site of action or used as biological probes.

=> s UDP-GalNAc
L8 2002 UDP-GALNAC

=> s l8 and glycoconjugate
L9 74 L8 AND GLYCOCONJUGATE

=> s l9 and ketone
L10 6 L9 AND KETONE

=> s l10 and galactose
L11   5 L10 AND GALACTOSE

=> dup remove l11
PROCESSING COMPLETED FOR L11
L12   1 DUP REMOVE L11 (4 DUPLICATES REMOVED)

=> d l12 cbib abs

L12 ANSWER 1 OF 1   MEDLINE on STN   DUPLICATE 1
2007347589.   PubMed ID: 17370997.   Direct identification of nonreducing
     GlcNAc residues on N-glycans of glycoproteins using a novel chemoenzymatic
     method. Boeggeman Elizabeth; Ramakrishnan Boopathy; Kilgore Charlton;
     Khidekel Nelly; Hsieh-Wilson Linda C; Simpson John T; Qasba Pradman K.
     (Structural Glycobiology Section, CCR-Nanobiology Program, Center for
     Cancer Research, NCI-Frederick, Frederick, Maryland 21702, USA.)
     Bioconjugate chemistry, (2007 May-Jun) Vol. 18, No. 3, pp. 806-14.
     Electronic Publication: 2007-03-20. Journal code: 9010319. ISSN:
     1043-1802. L-ISSN: 1043-1802. Pub. country: United States. Language:
     English.
AB   The mutant beta1,4-galactosyltransferase (beta4Gal-T1), beta4Gal-T1-Y289L,
     in contrast to wild-type beta4Gal-T1, can transfer GalNAc from the sugar
     donor **UDP-GalNAc** to the acceptor, GlcNAc, with
     efficiency as good as that of **galactose** from UDP-Gal.
     Furthermore, the mutant can also transfer a modified sugar, C2 keto
     galactose, from its UDP derivative to O-GlcNAc modification on
     proteins that provided a functional handle for developing a highly
     sensitive chemoenzymatic method for detecting O-GlcNAc post-translational
     modification on proteins. We report herein that the modified sugar, C2
     keto **galactose**, can be transferred to free GlcNAc residues on
     N-linked glycoproteins, such as ovalbumin or asialo-agalacto IgG1. The
     transfer is strictly dependent on the presence of both the mutant enzyme
     and the **ketone** derivative of the **galactose**. Moreover,
     the PNGase F treatment of the glycoproteins, which cleaves the N-linked
     oligosaccharide chain, shows that the modified sugar has been transferred
     to the N-glycan chains of the glycoproteins and not to the protein
     portion. The application of the mutant galactosyltransferase,
     beta4Gal-T1-Y289L, to produce **glycoconjugates** carrying sugar
     moieties with reactive groups, is demonstrated. We envision a broad
     potential for this technology such as the possibilities to link cargo
     molecules to glycoproteins, such as monoclonal antibodies, via glycan
     chains, thereby assisting in the glycotargeting of drugs to the site of
     action or used as biological probes.

=> s glyconjugate
L13   243 GLYCONJUGATE

=> s l13 and UDP galactose
L14   5 L13 AND UDP GALACTOSE

=> s l14 and C2
L15   0 L14 AND C2

=> s l14 and ketone
L16   0 L14 AND KETONE

=> dup remove l14
PROCESSING COMPLETED FOR L14
L17   1 DUP REMOVE L14 (4 DUPLICATES REMOVED)

=> d l17 cbib abs

L17 ANSWER 1 OF 1 MEDLINE on STN DUPLICATE 1
2004617602. PubMed ID: 15452127. srf-3, a mutant of Caenorhabditis elegans, resistant to bacterial infection and to biofilm binding, is deficient in glycoconjugates. Cipollo John F; Awad Antoine M; Costello Catherine E; Hirschberg Carlos B. (Department of Molecular and Cell Biology, Boston University, Goldman School of Dental Medicine, 715 Albany St., Boston, MA 02118-2526, USA.) The Journal of biological chemistry, (2004 Dec 17) Vol. 279, No. 51, pp. 52893-903. Electronic Publication: 2004-09-27. Journal code: 2985121R. ISSN: 0021-9258. L-ISSN: 0021-9258. Pub. country: United States. Language: English.

AB srf-3 is a mutant of C. elegans that is resistant to infection by Microbacterium nematophilum and to binding of the biofilm produced by Yersinia pseudotuberculosis and Yersinia pestis. Recently, SRF-3 was characterized as a nucleotide sugar transporter of the Golgi apparatus occurring exclusively in hypodermal seam cells, pharyngeal cells, and spermatheca. Based on the above observations, we hypothesized that srf-3 may have altered **glyconjugates** that may enable the mutant nematode to grow unaffected in the presence of the above pathogenic bacteria. Following analyses of N- and O-linked glycoconjugates of srf-3 and wild type nematodes using a combination of enzymatic degradation, permethylation, and mass spectrometry, we found in srf-3 a 65% reduction of acidic O-linked glycoconjugates containing glucuronic acid and galactose as well as a reduction of N-linked glycoconjugates containing galactose and fucose. These results are consistent with the specificity of SRF-3 for **UDP-galactose** and strongly suggest that the above glycoconjugates play an important role in allowing adhesion of M. nematophilum or Y. pseudotuberculosis biofilm to wild type C. elegans. Furthermore, because seam cells as well as pharyngeal cells secrete their glycoconjugates to the cuticle and surrounding surfaces, the results also demonstrate the critical role of these cells and their secreted glycoproteins in nematode-bacteria interactions and offer a mechanistic basis for strategies to block such recognition processes.

=> s (qasba p?/au or ramakrishnan b?/au)
L18 978 (QASBA P?/AU OR RAMAKRISHNAN B?/AU)

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L19 14 L18 AND CONJUGATE

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L20 1 L19 AND KETONE

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L20 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2010 ACS on STN
2007:321112 Document No. 146:517239 Direct Identification of Nonreducing GlcNAc Residues on N-Glycans of Glycoproteins Using a Novel Chemoenzymatic Method. Boeggeman, Elizabeth; **Ramakrishnan, Boopathy**; Kilgore, Charlton; Khidekel, Nelly; Hsieh-Wilson, Linda C.; Simpson, John T.; **Qasba, Pradman K.** (Structural Glycobiology Section, CCR-Nanobiology Program, Center for Cancer Research, NCI-Frederick, Frederick, MD, 21702, USA). Bioconjugate Chemistry, 18(3), 806-814 (English) 2007. CODEN: BCCHES. ISSN: 1043-1802. Publisher: American Chemical Society.

AB The mutant β1,4-galactosyltransferase (β4Gal-T1), β4Gal-T1-Y289L, in contrast to wild-type β4Gal-T1, can transfer GalNAc from the sugar donor UDP-GalNAc to the acceptor, GlcNAc, with efficiency as good as that of galactose from UDP-Gal. Furthermore, the mutant can also transfer a modified sugar, C2 keto galactose, from its UDP

derivative to O-GlcNAc modification on proteins that provided a functional handle for developing a highly sensitive chemoenzymic method for detecting O-GlcNAc post-translational modification on proteins. We report herein that the modified sugar, C2 keto galactose, can be transferred to free GlcNAc residues on N-linked glycoproteins, such as ovalbumin or asialo-agalacto IgG1. The transfer is strictly dependent on the presence of both the mutant enzyme and the **ketone** derivative of the galactose. Moreover, the PNGase F treatment of the glycoproteins, which cleaves the N-linked oligosaccharide chain, shows that the modified sugar has been transferred to the N-glycan chains of the glycoproteins and not to the protein portion. The application of the mutant galactosyltransferase, β4Gal-T1-Y289L, to produce glycoconjugates carrying sugar moieties with reactive groups, is demonstrated. We envision a broad potential for this technol. such as the possibilities to link cargo mols. to glycoproteins, such as monoclonal antibodies, via glycan chains, thereby assisting in the glyco-targeting of drugs to the site of action or used as biol. probes.

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L21 ANSWER 1 OF 7 HCAPLUS COPYRIGHT 2010 ACS on STN
2009:237398 Document No. 150:277401 Structure-based design of α1,3-N-acetylgalactosaminyltransferase from bovine α1,3 N-galactosyltransferase, and use in preparation of immunological compositions. **Qasba, Pradman K.; Ramakrishnan, Boopathy** ; Boeggeman, Elizabeth; Pasek, Marta (United States Dept. of Health and Human Services, USA). PCT Int. Appl. WO 2009025646 A1 20090226, 118pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IS, IT, LU, MC, ML, MR, MT, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2007-US18678 20070822.
AB The invention generally features compns. and methods based on the structure-based design of α1,3-N-Acetylgalactosaminyltransferase (α3 GalNAc-T) enzymes from bovine α1,3 galactosyltransferase (α3Gal-T) that can transfer 2'-modified galactose from the corresponding UDP-derivs. due to substitutions that broaden the α3Gal-T donor specificity and make the enzyme α3 GalNAc-T. The α3 GalNAc-T of the invention is in research and medicine, including in the development of imaging agents, diagnostic agents, pharmaceutical agents and improved vaccines that can be used to treat disease.

L21 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2010 ACS on STN
2009:239003 Document No. 150:277403 Structure-based design of β-1,4-galactosyltransferase I with altered donor and acceptor specificities, and use for preparing glycoconjugates for diagnostic and therapeutic applications. **Qasba, Pradman K.; Ramakrishnan, Boopathy**; Boeggeman, Elizabeth (United States Dept. of Health and Human Services, USA). PCT Int. Appl. WO 2009025645 A1 20090226, 108pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM,

KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IS, IT, LU, MC, ML, MR, MT, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2007-US18656 20070822.

AB The invention relates generally to human or bovine β-(1,4)-galactosyltransferase I mutants having altered donor and acceptor specificities, and methods of use thereof. In addition, the invention relates to methods for synthesizing oligosaccharides using the β-(1,4)-galactosyltransferase I mutants and to using the β-(1,4)- galactosyltransferase I mutants to **conjugate** agents, such as therapeutic agents or diagnostic agents, to acceptor mols. The glycoconjugates have use in disease treatment, diagnostic, and imaging.

L21 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2010 ACS on STN

2008:1449035 Document No. 150:17021 Cloning and sequence of human polypeptidyl-α- N-acetylgalactosaminyltransferase, and use in glycosylation and glycoconjugation. **Qasba, Pradman K.**; **Ramakrishnan, Boopathy** (United States Dept. of Health and Human Services, USA). PCT Int. Appl. WO 2008143944 A2 20081127, 69pp. DESIGNATED STATES: W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IS, IT, LU, MC, ML, MR, MT, NE, NL, NO, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2008-US6248 20080514. PRIORITY: US 2007-930294P 20070514.

AB The present invention provides isolated catalytic domains from a polypeptidyl-α- N-acetylgalactosaminyltransferase (pp-GalNAc-T). The invention also discloses the nucleotide sequence and the encoded amino acid sequence of the catalytic domain of human pp-GalNAc-T. The invention provides methods for engineering a glycoprotein from a biol. substrate, and methods for glycosylating a biol. substrate for use in glycoconjugation. Also included in the invention are diagnostic and therapeutic uses. The invention further provides in vitro folding methods for pp-GalNAc-T.

L21 ANSWER 4 OF 7 MEDLINE on STN DUPLICATE 1

2008368926. PubMed ID: 18426242. Site-specific linking of biomolecules via glycan residues using glycosyltransferases. **Qasba Pradman K**; Boeggeman Elizabeth; **Ramakrishnan Boopathy**. (Structural Glycobiology Section, SAIC-Frederick, Inc., Center for Cancer Research Nanobiology Program, Center for Cancer Research, NCI-Frederick, Frederick, Maryland 21702, USA.. qasba@helix.nih.gov) . Biotechnology progress, (2008 May-Jun) Vol. 24, No. 3, pp. 520-6. Electronic Publication: 2008-04-22. Ref: 42. Journal code: 8506292. E-ISSN: 1520-6033. L-ISSN: 1520-6033. Report No.: NLM-NIHMS46121; NLM-PMC2435414. Pub. country: United States. Language: English.

AB The structural information on glycosyltransferases has revealed that the sugar-donor specificity of these enzymes can be broadened to include modified sugars with a chemical handle that can be utilized for conjugation chemistry. Substitution of Tyr289 to Leu in the catalytic pocket of bovine beta-1,4-galactosyltransferase generates a novel glycosyltransferase that can transfer not only Gal but also GalNAc or a C2-modified galactose that has a chemical handle, from the corresponding UDP-derivatives, to the non-reducing end GlcNAc residue of a glycoconjugate. Similarly, the wild-type

polypeptide-N-acetyl-galactosaminyltransferase, which naturally transfers GalNAc from UDP-GalNAc, can also transfer C2-modified galactose with a chemical handle from its UDP-derivative to the Ser/Thr residue of a polypeptide acceptor substrate that is tagged as a fusion peptide to a non-glycoprotein. The potential of wild-type and mutant glycosyltransferases to produce glycoconjugates carrying sugar moieties with chemical handle makes it possible to **conjugate** biomolecules with orthogonal reacting groups at specific sites. This methodology assists in the assembly of bio-nanoparticles that are useful for developing targeted drug-delivery systems and contrast agents for magnetic resonance imaging.

L21 ANSWER 5 OF 7 MEDLINE on STN DUPLICATE 2
2008168516. PubMed ID: 18248315. Applications of glycosyltransferases in the site-specific conjugation of biomolecules and the development of a targeted drug delivery system and contrast agents for MRI.
Ramakrishnan Boopathy; Boeggeman Elizabeth; **Qasba Pradman K**. Expert opinion on drug delivery, (2008 Feb) Vol. 5, No. 2, pp. 149-53. Ref: 29. Journal code: 101228421. ISSN: 1742-5247. L-ISSN: 1742-5247.
Report No.: NLM-NIHMS44131; NLM-PMC2291282. Pub. country: England: United Kingdom. Language: English.
AB BACKGROUND: The delivery of drugs to the proposed site of action is a challenging task. Tissue and cell-specific guiding molecules are being used to carry a cargo of therapeutic molecules. The cargo molecules need to be conjugated in a site-specific manner to the therapeutic molecules such that the bioefficacy of these molecules is not compromised. METHODS: Using wild-type and mutant glycosyltransferases, the sugar moiety with a unique chemical handle is incorporated at a specific site in the cargo or therapeutic molecules, making it possible to **conjugate** these molecules through the chemical handle present on the modified glycan. RESULTS/CONCLUSIONS: The modified glycan residues introduced at specific sites on the cargo molecule make it possible to **conjugate** fluorophores for ELISA-based assays, radionuclides for imaging and immunotherapy applications, lipids for the assembly of immunoliposomes, cytotoxic drugs, cytokines, or toxins for antibody-based cancer therapy and the development of a targeted drug delivery system.

L21 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2010 ACS on STN
2007:321112 Document No. 146:517239 Direct Identification of Nonreducing GlcNAc Residues on N-Glycans of Glycoproteins Using a Novel Chemoenzymatic Method. Boeggeman, Elizabeth; **Ramakrishnan, Boopathy**; Kilgore, Charlton; Khidekel, Nelly; Hsieh-Wilson, Linda C.; Simpson, John T.; **Qasba, Pradman K.** (Structural Glycobiology Section, CCR-Nanobiology Program, Center for Cancer Research, NCI-Frederick, Frederick, MD, 21702, USA). Bioconjugate Chemistry, 18(3), 806-814 (English) 2007. CODEN: BCCHES. ISSN: 1043-1802. Publisher: American Chemical Society.
AB The mutant β1,4-galactosyltransferase (β4Gal-T1), β4Gal-T1-Y289L, in contrast to wild-type β4Gal-T1, can transfer GalNAc from the sugar donor UDP-GalNAc to the acceptor, GlcNAc, with efficiency as good as that of galactose from UDP-Gal. Furthermore, the mutant can also transfer a modified sugar, C2 keto galactose, from its UDP derivative to O-GlcNAc modification on proteins that provided a functional handle for developing a highly sensitive chemoenzymic method for detecting O-GlcNAc post-translational modification on proteins. We report herein that the modified sugar, C2 keto galactose, can be transferred to free GlcNAc residues on N-linked glycoproteins, such as ovalbumin or asialo-agalacto IgG1. The transfer is strictly dependent on the presence of both the mutant enzyme and the ketone derivative of the galactose. Moreover, the PNGase F treatment of the glycoproteins, which cleaves the N-linked oligosaccharide chain, shows that the modified sugar has been

transferred to the N-glycan chains of the glycoproteins and not to the protein portion. The application of the mutant galactosyltransferase, β4Gal-T1-Y289L, to produce glycoconjugates carrying sugar moieties with reactive groups, is demonstrated. We envision a broad potential for this technol. such as the possibilities to link cargo mols. to glycoproteins, such as monoclonal antibodies, via glycan chains, thereby assisting in the glyco-targeting of drugs to the site of action or used as biol. probes.

L21 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2010 ACS on STN
2005:490304 Document No. 143:48058 Targeted delivery system for bioactive agents. **Qasba, Pradman; Ramakrishnan, Boopathy** (United States Dept. of Health and Human Services, USA). PCT Int. Appl. WO 2005051429 A2 20050609, 63 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IS, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-US38781 20041118. PRIORITY: US 2003-523112P 20031119.

AB In accordance with the present invention, compds., compns. and methods are provided that allow for the administration of a bioactive agent to an organism, including a human or an animal. The present invention can be used to treat or prevent a disease and/or disorder with a bioactive agent, or can be used to safely vaccinate a human or animal against a bioactive agent. The invention can also be used as a method for the delivery of bioactive agents for the treatment or prevention of a disease and/or a disorder, particularly targeted delivery of bioactive agents through the administration of glycoconjugates containing a bioactive agent bound to a targeting compound through a modified saccharide residue. A chemoenzymic approach toward the rapid and sensitive detection of O-GlcNAc posttranslational modifications is also described.

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